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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY -(PCT)

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<p>(21) International Application Number: PCT/CA97/00829</p> <p>(22) International Filing Date: 4 November 1997 (04.11.97)</p> <p>(30) Priority Data: 08/743,637 4 November 1996 (04.11.96) US</p> <p>(71) Applicant (<i>for all designated States except US</i>): INFECTIO DIAGNOSTIC (I.D.I.) INC. [CA/CA]; 4<sup>eme</sup> étage, 2050, boulevard René Lévesque Ouest, Sainte-Foy, Québec G1V 2K8 (CA).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (<i>for US only</i>): BERGERON, Michel, G. [CA/CA]; 2069, rue Brûlard, Sillery, Québec G1T 1G2 (CA). PICARD, François, J. [CA/CA]; 1245, rue de la Sapinière, Cap-Rouge, Québec G1Y 1A1 (CA). OUELLETTE, Marc [CA/CA]; 1035 de Ploermele, Sillery, Québec G1S 3S1 (CA). ROY, Paul, H. [US/US]; 28, rue Charles Garnier, Loretteville, Québec G2A 2X8 (CA).</p> <p>(74) Agents: DUBUC, Jean, H. et al.; Goudreau Gage Dubuc &amp; Martineau Walker, The Stock Exchange Tower, Suite 3400, 800 Place Victoria, P.O. Box 242, Montreal, Québec H4Z 1E9 (CA).</p>			<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b> <i>Without international search report and to be republished upon receipt of that report.</i></p>
<p>(54) Title: SPECIES-SPECIFIC, GENUS-SPECIFIC AND UNIVERSAL DNA PROBES AND AMPLIFICATION PRIMERS TO RAPIDLY DETECT AND IDENTIFY COMMON BACTERIAL AND FUNGAL PATHOGENS AND ASSOCIATED ANTIOTIC RESISTANCE GENES FROM CLINICAL SPECIMENS FOR DIAGNOSIS IN MICROBIOLOGY LABORATORIES</p> <p>(57) Abstract</p> <p>DNA-based methods employing amplification primers or probes for detecting, identifying, and quantifying in a test sample DNA from (i) any bacterium, (ii) the species <i>Streptococcus agalactiae</i>, <i>Staphylococcus saprophyticus</i>, <i>Enterococcus faecium</i>, <i>Neisseria meningitidis</i>, <i>Listeria monocytogenes</i> and <i>Candida albicans</i>, and (iii) any species of the genera <i>Streptococcus</i>, <i>Staphylococcus</i>, <i>Enterococcus</i>, <i>Neisseria</i> and <i>Candida</i> are disclosed. DNA-based methods employing amplification primers or probes for detecting, identifying, and quantifying in a test sample antibiotic resistance genes selected from the group consisting of <i>bla<sub>tem</sub></i>, <i>bla<sub>rob</sub></i>, <i>bla<sub>shv</sub></i>, <i>bla<sub>oxa</sub></i>, <i>bla<sub>Z</sub></i>, <i>aadB</i>, <i>aacC1</i>, <i>aacC2</i>, <i>aacC3</i>, <i>aacA4</i>, <i>aac<sup>6'-Ila</sup></i>, <i>ermA</i>, <i>ermB</i>, <i>ermC</i>, <i>mecA</i>, <i>vanA</i>, <i>vanB</i>, <i>vanC</i>, <i>satA</i>, <i>aac(6'-aph(2'))</i>, <i>aad(6')</i>, <i>vat</i>, <i>vga</i>, <i>msrA</i>, <i>sul</i> and <i>int</i> are also disclosed. The above microbial species, genera and resistance genes are all clinically relevant and commonly encountered in a variety of clinical specimens. These DNA-based assays are rapid, accurate and can be used in clinical microbiology laboratories for routine diagnosis. These novel diagnostic tools should be useful to improve the speed and accuracy of diagnosis of microbial infections, thereby allowing more effective treatments. Diagnostic kits for (i) the universal detection and quantification of bacteria, and/or (ii) the detection, identification and quantification of the above-mentioned bacterial and fungal species and/or genera, and/or (iii) the detection, identification and quantification of the above-mentioned antibiotic resistance genes are also claimed.</p>			

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**TITLE OF THE INVENTION**

SPECIES-SPECIFIC, GENUS-SPECIFIC AND UNIVERSAL DNA PROBES AND  
AMPLIFICATION PRIMERS TO RAPIDLY DETECT AND IDENTIFY COMMON  
BACTERIAL AND FUNGAL PATHOGENS AND ASSOCIATED ANTIBIOTIC  
5 RESISTANCE GENES FROM CLINICAL SPECIMENS FOR DIAGNOSIS IN  
MICROBIOLOGY LABORATORIES

**BACKGROUND OF THE INVENTION****Classical methods for the identification and susceptibility testing of bacteria**

10 Bacteria are classically identified by their ability to utilize different substrates as a source of carbon and nitrogen through the use of biochemical tests such as the API20E™ system (bioMérieux). For susceptibility testing, clinical microbiology laboratories use methods including disk diffusion, agar dilution and broth microdilution. Although identifications based on biochemical tests and antibacterial susceptibility  
15 tests are cost-effective, at least two days are required to obtain preliminary results due to the necessity of two successive overnight incubations to identify the bacteria from clinical specimens as well as to determine their susceptibility to antimicrobial agents. There are some commercially available automated systems (i.e. the MicroScan system from Dade Diagnostics Corp. and the Vitek system from bioMérieux) which use  
20 sophisticated and expensive apparatus for faster microbial identification and susceptibility testing (Stager and Davis, 1992, Clin. Microbiol. Rev. 5:302-327). These systems require shorter incubation periods, thereby allowing most bacterial identifications and susceptibility testing to be performed in less than 6 hours. Nevertheless, these faster systems always require the primary isolation of the bacteria  
25 as a pure culture, a process which takes at least 18 hours for a pure culture or 2 days for a mixed culture. The fastest identification system, the autoSCAN-Walk-Away™ system (Dade Diagnostics Corp.) identifies both gram-negative and gram-positive bacterial species from standardized inoculum in as little as 2 hours and gives susceptibility patterns to most antibiotics in 5.5 hours. However, this system has a  
30 particularly high percentage (i.e. 3.3 to 40.5%) of non-conclusive identifications with bacterial species other than *Enterobacteriaceae* (Croizé J., 1995, Lett. Infectiol. 10:109-113; York *et al.*, 1992, J. Clin. Microbiol. 30:2903-2910). For *Enterobacteriaceae*, the percentage of non-conclusive identifications was 2.7 to 11.4%.

35 A wide variety of bacteria and fungi are routinely isolated and identified from clinical specimens in microbiology laboratories. Tables 1 and 2 give the incidence for the most commonly isolated bacterial and fungal pathogens from various types of clinical specimens. These pathogens are the most frequently associated with nosocomial and community-acquired human infections and are therefore considered the most clinically important.

### Clinical specimens tested in clinical microbiology laboratories

Most clinical specimens received in clinical microbiology laboratories are urine and blood samples. At the microbiology laboratory of the Centre Hospitalier de l'Université Laval (CHUL), urine and blood account for approximately 55% and 30% of the specimens received, respectively (Table 3). The remaining 15% of clinical specimens comprise various biological fluids including sputum, pus, cerebrospinal fluid, synovial fluid, and others (Table 3). Infections of the urinary tract, the respiratory tract and the bloodstream are usually of bacterial etiology and require antimicrobial therapy. In fact, all clinical samples received in the clinical microbiology laboratory are tested routinely for the identification of bacteria and susceptibility testing.

### Conventional pathogen identification from clinical specimens

#### **Urine specimens**

The search for pathogens in urine specimens is so preponderant in the routine microbiology laboratory that a myriad of tests have been developed. However, the gold standard remains the classical semi-quantitative plate culture method in which 1  $\mu$ L of urine is streaked on plates and incubated for 18-24 hours. Colonies are then counted to determine the total number of colony forming units (CFU) per liter of urine. A bacterial urinary tract infection (UTI) is normally associated with a bacterial count of  $10^7$  CFU/L or more in urine. However, infections with less than  $10^7$  CFU/L in urine are possible, particularly in patients with a high incidence of diseases or those catheterized (Stark and Maki, 1984, *N. Engl. J. Med.* 311:560-564). Importantly, approximately 80% of urine specimens tested in clinical microbiology laboratories are considered negative (i.e. bacterial count of less than  $10^7$  CFU/L; Table 3). Urine specimens found positive by culture are further characterized using standard biochemical tests to identify the bacterial pathogen and are also tested for susceptibility to antibiotics. The biochemical and susceptibility testing normally require 18-24 hours of incubation.

Accurate and rapid urine screening methods for bacterial pathogens would allow a faster identification of negative specimens and a more efficient treatment and care management of patients. Several rapid identification methods (Uriscreen™, UTIscreen™, Flash Track™ DNA probes and others) have been compared to slower standard biochemical methods, which are based on culture of the bacterial pathogens. Although much faster, these rapid tests showed low sensitivities and poor specificities as well as a high number of false negative and false positive results (Koenig *et al.*, 1992, *J. Clin. Microbiol.* 30:342-345; Pezzlo *et al.*, 1992, *J. Clin. Microbiol.* 30:640-684).

#### **Blood specimens**

The blood specimens received in the microbiology laboratory are always submitted for culture. Blood culture systems may be manual, semi-automated or completely automated. The BACTEC system (from Becton Dickinson) and the

BacTAlert system (from Organon Teknica Corporation) are the two most widely used automated blood culture systems. These systems incubate blood culture bottles under optimal conditions for bacterial growth. Bacterial growth is monitored continuously to detect early positives by using highly sensitive bacterial growth detectors. Once growth is detected, a Gram stain is performed directly from the blood culture and then used to inoculate nutrient agar plates. Subsequently, bacterial identification and susceptibility testing are carried out from isolated bacterial colonies with automated systems as described previously. The bottles are normally reported as negative if no growth is detected after an incubation of 6 to 7 days. Normally, the vast majority of blood cultures are reported negative. For example, the percentage of negative blood cultures at the microbiology laboratory of the CHUL for the period February 1994-January 1995 was 93.1% (Table 3).

#### **Other clinical samples**

Upon receipt by the clinical microbiology laboratory, all body fluids other than blood and urine that are from normally sterile sites (i.e. cerebrospinal, synovial, pleural, pericardial and others) are processed for direct microscopic examination and subsequent culture. Again, most clinical samples are negative for culture (Table 3).

Regarding clinical specimens which are not from sterile sites such as sputum or stool specimens, the laboratory diagnosis by culture is more problematic because of the contamination by the normal flora. The bacterial pathogens potentially associated with the infection are purified from the contaminants and then identified as described previously. Of course, the universal detection of bacteria would not be useful for the diagnosis of bacterial infections at these non sterile sites. On the other hand, DNA-based assays for species or genus detection and identification as well as for the detection of antibiotic resistance genes from these specimens would be very useful and would offer several advantages over classical identification and susceptibility testing methods.

#### **DNA-based assays with any clinical specimens**

There is an obvious need for rapid and accurate diagnostic tests for bacterial detection and identification directly from clinical specimens. DNA-based technologies are rapid and accurate and offer a great potential to improve the diagnosis of infectious diseases (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.). The DNA probes and amplification primers which are objects of the present invention are applicable for bacterial or fungal detection and identification directly from any clinical specimens such as blood cultures, blood, urine, sputum, cerebrospinal fluid, pus and other type of specimens (Table 3). The DNA-based tests proposed in this invention are superior in terms of both rapidity and accuracy to standard biochemical methods currently used for routine diagnosis from any clinical specimens in microbiology laboratories. Since

these tests are performed in around only one hour, they provide the clinicians with new diagnostic tools which should contribute to increase the efficiency of therapies with antimicrobial agents. Clinical specimens from organisms other than humans (e.g. other primates, birds, plants, mammals, farm animals, livestock and others) may also be  
5 tested with these assays.

**A high percentage of culture negative specimens**

Among all the clinical specimens received for routine diagnosis, approximately 80% of urine specimens and even more (around 95%) for other types of clinical specimens are negative for the presence of bacterial pathogens (Table 3). It would  
10 also be desirable, in addition to identify bacteria at the species or genus level in a given specimen, to screen out the high proportion of negative clinical specimens with a test detecting the presence of any bacterium (i.e. universal bacterial detection). Such a screening test may be based on the DNA amplification by PCR of a highly conserved  
15 genetic target found in all bacteria. Specimens negative for bacteria would not be amplified by this assay. On the other hand, those that are positive for bacteria would give a positive amplification signal with this assay.

**Towards the development of rapid DNA-based diagnostic tests**

A rapid diagnostic test should have a significant impact on the management of infections. DNA probe and DNA amplification technologies offer several advantages  
20 over conventional methods for the identification of pathogens and antibiotic resistance genes from clinical samples (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.; Ehrlich and Greenberg, 1994, PCR-based Diagnostics in Infectious Disease, Blackwell Scientific Publications, Boston, MA). There is no need for culture of the bacterial  
25 pathogens, hence the organisms can be detected directly from clinical samples, thereby reducing the time associated with the isolation and identification of pathogens. Furthermore, DNA-based assays are more accurate for bacterial identification than currently used phenotypic identification systems which are based on biochemical tests. Commercially available DNA-based technologies are currently used in clinical  
30 microbiology laboratories, mainly for the detection and identification of fastidious bacterial pathogens such as *Mycobacterium tuberculosis*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae* as well as for the detection of a variety of viruses (Podzorski and Persing, Molecular detection and identification of microorganisms, *In* : P. Murray *et al.*, 1995, Manual of Clinical Microbiology, ASM press, Washington D.C.). There are  
35 also other commercially available DNA-based assays which are used for culture confirmation assays.

Others have developed DNA-based tests for the detection and identification of bacterial pathogens which are objects of the present invention: *Staphylococcus* spp. (US patent application serial No. US 5 437 978), *Neisseria* spp. (US patent application

5 serial No. US 5 162 199 and European patent application serial No. EP 0 337 896 131) and *Listeria monocytogenes* (US patent applications serial Nos US 5 389 513 and US 5 089 386). However, the diagnostic tests described in these patents are based either on rRNA genes or on genetic targets different from those described in the present invention.

10 Although there are diagnostic kits or methods already used in clinical microbiology laboratories, there is still a need for an advantageous alternative to the conventional culture identification methods in order to improve the accuracy and the speed of the diagnosis of commonly encountered bacterial infections. Besides being 15 much faster, DNA-based diagnostic tests are more accurate than standard biochemical tests presently used for diagnosis because the bacterial genotype (e.g. DNA level) is more stable than the bacterial phenotype (e.g. metabolic level).

15 Knowledge of the genomic sequences of bacterial and fungal species continuously increases as testified by the number of sequences available from databases. From the sequences readily available from databases, there is no indication therefrom as to their potential for diagnostic purposes. For determining good candidates for diagnostic purposes, one could select sequences for DNA-based assays for (i) the species-specific detection and identification of commonly 20 encountered bacterial or fungal pathogens, (ii) the genus-specific detection and identification of commonly encountered bacterial or fungal pathogens, (iii) the universal detection of bacterial or fungal pathogens and/or (iv) the specific detection and identification of antibiotic resistance genes. All of the above types of DNA-based assays may be performed directly from any type of clinical specimens or from a microbial culture.

25 In our co-pending U.S. (N.S. 08/526,840) and PCT (PCT/CA/95/00528) patent applications, we described DNA sequences suitable for (i) the species-specific detection and identification of 12 clinically important bacterial pathogens, (ii) the universal detection of bacteria, and (iii) the detection of 17 antibiotic resistance genes. This co-pending application described proprietary DNA sequences and DNA 30 sequences selected from databases (in both cases, fragments of at least 100 base pairs), as well as oligonucleotide probes and amplification primers derived from these sequences. All the nucleic acid sequences described in this patent application enter the composition of diagnostic kits and methods capable of a) detecting the presence of bacteria, b) detecting specifically the presence of 12 bacterial species and 17 35 antibiotic resistance genes. However, these methods and kits need to be improved, since the ideal kit and method should be capable of diagnosing close to 100% of microbial pathogens and antibiotic resistance genes. For example, infections caused by *Enterococcus faecium* have become a clinical problem because of its resistance to many antibiotics. Both the detection of these bacteria and the evaluation of their

resistance profiles are desirable. Besides that, novel DNA sequences (probes and primers) capable of recognizing the same and other microbial pathogens or the same and additional antibiotic resistance genes are also desirable to aim at detecting more target genes and complement our earlier patent application.

5

### **STATEMENT OF THE INVENTION**

It is an object of the present invention to provide a specific, ubiquitous and sensitive method using probes and/or amplification primers for determining the presence and/or amount of nucleic acids:

10 - from specific microbial species or genera selected from the group consisting of *Streptococcus* species, *Streptococcus agalactiae*, *Staphylococcus* species, *Staphylococcus saprophyticus*, *Enterococcus* species, *Enterococcus faecium*, *Neisseria* species, *Neisseria meningitidis*, *Listeria monocytogenes*, *Candida* species and *Candida albicans*

15 - from an antibiotic resistance gene selected from the group consisting of *bla<sub>tem</sub>*, *bla<sub>rob</sub>*, *bla<sub>shv</sub>*, *bla<sub>oxa</sub>*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aacA4*, *aac6'-Ila*, *ermA*, *ermB*, *ermC*, *mecA*, *vanA*, *vanB*, *vanC*, *satA*, *aac(6')-aph(2")*, *aad(6')*, *vat*, *vga*, *msrA*, *sul* and *int*, and optionally,

- from any bacterial species

20 in any sample suspected of containing said nucleic acids,  
wherein each of said nucleic acids or a variant or part thereof comprises a selected target region hybridizable with said probe or primers;

25 said method comprising the steps of contacting said sample with said probes or primers and detecting the presence and/or amount of hybridized probes or amplified products as an indication of the presence and/or amount of said any bacterial species, specific microbial species or genus and antibiotic resistance gene.

In a specific embodiment, a similar method directed to each specific microbial species or genus detection and identification, antibiotic resistance genes detection, and universal bacterial detection, separately, is provided.

30 In a more specific embodiment, the method makes use of DNA fragments (proprietary fragments and fragments obtained from databases), selected for their capacity to sensitively, specifically and ubiquitously detect the targeted bacterial or fungal nucleic acids.

35 In a particularly preferred embodiment, oligonucleotides of at least 12 nucleotides in length have been derived from the longer DNA fragments, and are used in the present method as probes or amplification primers.

The proprietary oligonucleotides (probes and primers) are also another object of the invention.

Diagnostic kits comprising probes or amplification primers for the detection of

a microbial species or genus selected from the group consisting of *Streptococcus* species, *Streptococcus agalactiae*, *Staphylococcus* species, *Staphylococcus saprophyticus*, *Enterococcus* species, *Enterococcus faecium*, *Neisseria* species, *Neisseria meningitidis*, *Listeria monocytogenes*, *Candida* species and *Candida albicans* are also objects of the present invention.

5 Diagnostic kits further comprising probes or amplification primers for the detection of an antibiotic resistance gene selected from the group consisting of *bla<sub>tem</sub>*, *bla<sub>rbp</sub>*, *bla<sub>shv</sub>*, *bla<sub>oxb</sub>*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aacA4*, *aac6'-Ila*, *ermA*, *ermB*, *ermC*, *mecA*, *vanA*, *vanB*, *vanC*, *satA*, *aac(6')-aph(2")*, *aad(6')*, *vat*, *vga*, *msrA*, *sul* and *int* are also objects of this invention.

10 Diagnostic kits further comprising probes or amplification primers for the detection of any bacterial or fungal species, comprising or not comprising those for the detection of the specific microbial species or genus listed above, and further comprising or not comprising probes and primers for the antibiotic resistance genes listed above, are also objects of this invention.

15 In a preferred embodiment, such a kit allows for the separate or the simultaneous detection and identification of the above-listed microbial species or genus, antibiotic resistance genes and for the detection of any bacterium.

In the above methods and kits, amplification reactions may include a) 20 polymerase chain reaction (PCR), b) ligase chain reaction, c) nucleic acid sequence-based amplification, d) self-sustained sequence replication, e) strand displacement amplification, f) branched DNA signal amplification, g) transcription-mediated amplification, h) cycling probe technology (CPT) i) nested PCR, or j) multiplex PCR.

In a preferred embodiment, a PCR protocol is used as an amplification reaction. 25 In a particularly preferred embodiment, a PCR protocol is provided, comprising, for each amplification cycle, an annealing step of 30 seconds at 45-55°C and a denaturation step of only one second at 95°C, without any time allowed specifically for the elongation step. This PCR protocol has been standardized to be suitable for PCR reactions with all selected primer pairs, which greatly facilitates the testing because 30 each clinical sample can be tested with universal, species-specific, genus-specific and antibiotic resistance gene PCR primers under uniform cycling conditions. Furthermore, various combinations of primer pairs may be used in multiplex PCR assays.

We aim at developing a rapid test or kit to discard rapidly all the samples which 35 are negative for bacterial cells and to subsequently detect and identify the above bacterial and/or fungal species and genera and to determine rapidly the bacterial resistance to antibiotics. Although the sequences from the selected antibiotic resistance genes are available from databases and have been used to develop DNA-based tests for their detection, our approach is unique because it represents a major improvement over current gold standard diagnostic methods based on bacterial

5       cultures. Using an amplification method for the simultaneous bacterial detection and identification and antibiotic resistance genes detection, there is no need for culturing the clinical sample prior to testing. Moreover, a modified PCR protocol has been developed to detect all target DNA sequences in approximately one hour under uniform amplification conditions. This procedure will save lives by optimizing treatment, will diminish antibiotic resistance because less antibiotics will be prescribed, will reduce the use of broad spectrum antibiotics which are expensive, decrease overall health care costs by preventing or shortening hospitalizations, and decrease the time and costs associated with clinical laboratory testing.

10       In the methods and kits described herein below, the oligonucleotide probes and amplification primers have been derived from larger sequences (i.e. DNA fragments of at least 100 base pairs). All DNA fragments have been obtained either from proprietary fragments or from databases. DNA fragments selected from databases are newly used in a method of detection according to the present invention, since they 15       have been selected for their diagnostic potential.

15       It is clear to the individual skilled in the art that other oligonucleotide sequences appropriate for (i) the universal bacterial detection, (ii) the detection and identification of the above microbial species or genus and (iii) the detection of antibiotic resistance genes other than those listed in Annex VI may also be derived from the proprietary 20       fragments or selected database sequences. For example, the oligonucleotide primers or probes may be shorter or longer than the ones we have chosen; they may also be selected anywhere else in the proprietary DNA fragments or in the sequences selected from databases; they may be also variants of the same oligonucleotide. If the target DNA or a variant thereof hybridizes to a given oligonucleotide, or if the target DNA or 25       a variant thereof can be amplified by a given oligonucleotide PCR primer pair, the converse is also true; a given target DNA may hybridize to a variant oligonucleotide probe or be amplified by a variant oligonucleotide PCR primer. Alternatively, the oligonucleotides may be designed from any DNA fragment sequences for use in amplification methods other than PCR. Consequently, the core of this invention is the 30       identification of universal, species-specific, genus-specific and resistance gene-specific genomic or non-genomic DNA fragments which are used as a source of specific and ubiquitous oligonucleotide probes and/or amplification primers. Although the selection and evaluation of oligonucleotides suitable for diagnostic purposes requires much effort, it is quite possible for the individual skilled in the art to derive, from the selected 35       DNA fragments, oligonucleotides other than the ones listed in Annex VI which are suitable for diagnostic purposes. When a proprietary fragment or a database sequence is selected for its specificity and ubiquity, it increases the probability that subsets thereof will also be specific and ubiquitous.

Since a high percentage of clinical specimens are negative for bacteria (Table

3), DNA fragments having a high potential for the selection of universal oligonucleotide probes or primers were selected from proprietary and database sequences. The amplification primers were selected from a gene highly conserved in bacteria and fungi, and are used to detect the presence of any bacterial pathogen in clinical 5 specimens in order to determine rapidly (approximately one hour) whether it is positive or negative for bacteria. The selected gene, designated *tuf*, encodes a protein (EF-Tu) involved in the translational process during protein synthesis. The *tuf* gene sequence alignments used to derive the universal primers include both proprietary and database sequences (Example 1 and Annex I). This strategy allows the rapid screening of the 10 numerous negative clinical specimens (around 80% of the specimens received, see Table 3) submitted for bacteriological testing. Tables 4, 5 and 6 provide a list of the bacterial or fungal species used to test the specificity of PCR primers and DNA probes. Table 7 gives a brief description of each species-specific, genus-specific and universal 15 amplification assays which are objects of the present invention. Tables 8, 9 and 10 provide some relevant information about the proprietary and database sequences selected for diagnostic purposes.

#### **DETAILED DESCRIPTION OF THE INVENTION**

**Development of species-specific, genus-specific, universal and antibiotic 20 resistance gene-specific DNA probes and amplification primers for microorganisms**

##### **Selection from databases of sequences suitable for diagnostic purposes**

In order to select sequences which are suitable for species-specific or genus-specific detection and identification of bacteria or fungi or, alternatively, for the 25 universal detection of bacteria, the database sequences (GenBank, EMBL and Swiss-Prot) were chosen based on their potential for diagnostic purposes according to sequence information and computer analysis performed with these sequences. Initially, all sequence data available for the targeted microbial species or genus were carefully analyzed. The gene sequences which appeared the most promising for diagnostic 30 purposes based on sequence information and on sequence comparisons with the corresponding gene in other microbial species or genera performed with the Genetics Computer Group (GCG, Wisconsin) programs were selected for testing by PCR. Optimal PCR amplification primers were chosen from the selected database sequences with the help of the Oligo™ 4.0 primer analysis software (National 35 Biosciences Inc., Plymouth, Minn.). The chosen primers were tested in PCR assays for their specificity and ubiquity for the target microbial species or genus. In general, the identification of database sequences from which amplification primers suitable for species-specific or genus-specific detection and identification were selected involved the computer analysis and PCR testing of several candidate gene sequences before

obtaining a primer pair which is specific and ubiquitous for the target microbial species or genus. Annex VI provides a list of selected specific and ubiquitous PCR primer pairs. Annexes I to V and Examples 1 to 4 illustrate the strategy used to select genus-specific, species-specific and universal PCR primers from *tuf* sequences or from the 5 *recA* gene.

**Oligonucleotide primers and probes design and synthesis**

The DNA fragments sequenced by us or selected from databases (GenBank and EMBL) were used as sources of oligonucleotides for diagnostic purposes. For this 10 strategy, an array of suitable oligonucleotide primers or probes derived from a variety of genomic DNA fragments (size of more than 100 bp) selected from databases were tested for their specificity and ubiquity in PCR and hybridization assays as described later. It is important to note that the database sequences were selected based on their 15 potential for being species-specific, genus-specific or universal for the detection of bacteria or fungi according to available sequence information and extensive analysis and that, in general, several candidate database sequences had to be tested in order to obtain the desired specificity, ubiquity and sensitivity.

Oligonucleotide probes and amplification primers derived from species-specific 20 fragments selected from database sequences were synthesized using an automated DNA synthesizer (Perkin-Elmer Corp., Applied Biosystems Division). Prior to synthesis, all oligonucleotides (probes for hybridization and primers for DNA amplification) were evaluated for their suitability for hybridization or DNA amplification by polymerase 25 chain reaction (PCR) by computer analysis using standard programs (i.e. the Genetics Computer Group (GCG) programs and the primer analysis software Oligo™ 4.0). The potential suitability of the PCR primer pairs was also evaluated prior to the synthesis by verifying the absence of unwanted features such as long stretches of one nucleotide and a high proportion of G or C residues at the 3' end (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.).

The oligonucleotide primers or probes may be derived from either strand of the 30 duplex DNA. The primers or probes may consist of the bases A, G, C, or T or analogs and they may be degenerated at one or more chosen nucleotide position(s). The primers or probes may be of any suitable length and may be selected anywhere within the DNA sequences from proprietary fragments or from selected database sequences which are suitable for (i) the universal detection of bacteria, (ii) the species-specific 35 detection and identification of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae* and *Candida albicans* (iii) the genus-specific detection of *Streptococcus* species, *Enterococcus* species, *Staphylococcus* species and *Neisseria* species or (iv) the detection of the 26 above-mentioned clinically important antibiotic resistance genes.

Variants for a given target bacterial gene are naturally occurring and are attributable to sequence variation within that gene during evolution (Watson *et al.*, 1987, Molecular Biology of the Gene, 4<sup>th</sup> ed., The Benjamin/Cummings Publishing Company, Menlo Park, CA; Lewin, 1989, Genes IV, John Wiley & Sons, New York, NY). For example, different strains of the same bacterial species may have a single or more nucleotide variation(s) at the oligonucleotide hybridization site. The person skilled in the art is well aware of the existence of variant bacterial or fungal DNA sequences for a specific gene and that the frequency of sequence variations depends on the selective pressure during evolution on a given gene product. The detection of a variant sequence for a region between two PCR primers may be demonstrated by sequencing the amplification product. In order to show the presence of sequence variants at the primer hybridization site, one has to amplify a larger DNA target with PCR primers outside that hybridization site. Sequencing of this larger fragment will allow the detection of sequence variation at this site. A similar strategy may be applied to show variants at the hybridization site of a probe. Insofar as the divergence of the target sequences or a part thereof does not affect the specificity and ubiquity of the amplification primers or probes, variant bacterial DNA is under the scope of this invention. Variants of the selected primers or probes may also be used to amplify or hybridize to a variant DNA.

**20 Sequencing of *tuf* sequences from a variety of bacterial and fungal species**

The nucleotide sequence of a portion of *tuf* genes was determined for a variety of bacterial and fungal species. The amplification primers SEQ ID NOs: 107 and 108, which amplify a *tuf* gene portion of approximately 890 bp, were used for the sequencing of bacterial *tuf* sequences. The amplification primers SEQ ID NOs: 109 and 172, which amplify a *tuf* gene portion of approximately 830 bp, were used for the sequencing of fungal *tuf* sequences. Both primer pairs can amplify *tufA* and *tufB* genes. This is not surprising because these two genes are nearly identical. For example, the entire *tufA* and *tufB* genes from *E. coli* differ at only 13 nucleotide positions (Neidhardt *et al.*, 1996, *Escherichia coli* and *Salmonella*: Cellular and Molecular Biology, 2<sup>nd</sup> ed., American Society for Microbiology Press, Washington, D.C.). These amplification primers are degenerated at several nucleotide positions and contain inosines in order to allow the amplification of a wide range of *tuf* sequences. The strategy used to select these amplification primers is similar to that illustrated in Annex I for the selection of universal primers. The amplification primers SEQ ID NOs: 107 and 108 could be used to amplify the *tuf* genes from any bacterial species. The amplification primers SEQ ID NOs: 109 and 172 could be used to amplify the *tuf* genes from any fungal species.

The *tuf* genes were amplified directly from bacterial or yeast cultures using the following amplification protocol: One  $\mu$ L of cell suspension was transferred directly to

19  $\mu$ L of a PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl<sub>2</sub>, 1  $\mu$ M of each of the 2 primers, 200  $\mu$ M of each of the four dNTPs, 0.5 unit of *Taq* DNA polymerase (Promega Corp., Madison, WI). PCR reactions were subjected to cycling using a MJ Research PTC-200 thermal cycler (MJ 5 Research Inc., Watertown, Mass.) as follows: 3 min at 96°C followed by 30-35 cycles of 1 min at 95°C for the denaturation step, 1 min at 30-50°C for the annealing step and 1 min at 72°C for the extension step. Subsequently, twenty microliters of the PCR-amplified mixture were resolved by electrophoresis in a 1.5% agarose gel. The gel was then visualized by staining with methylene blue (Flores *et al.*, 1992, *Biotechniques*, 10:203-205). The size of the amplification products was estimated by comparison with a 100-bp molecular weight ladder. The band corresponding to the specific amplification product (i.e. approximately 890 or 830 bp for bacterial or fungal *tuf* sequences, respectively) was excised from the agarose gel and purified using the QIAquick™ gel extraction kit (QIAGEN Inc., Chatsworth, CA). The gel-purified DNA fragment was then 10 used directly in the sequencing protocol. Both strands of the *tuf* genes amplification product were sequenced by the dideoxynucleotide chain termination sequencing method by using an Applied Biosystems automated DNA sequencer (model 373A) with their PRISM™ Sequenase® Terminator Double-stranded DNA Sequencing Kit (Perkin- 15 Elmer Corp., Applied Biosystems Division, Foster City, CA). The sequencing reactions 20 were all performed by using the amplification primers (SEQ ID NOs: 107 to 109 and 172) and 100 ng per reaction of the gel-purified amplicon. In order to ensure that the determined sequence did not contain errors attributable to the sequencing of PCR artefacts, we have sequenced two preparations of the gel-purified *tuf* amplification product originating from two independent PCR amplifications. For all target microbial 25 species, the sequences determined for both amplicon preparations were identical. Furthermore, the sequences of both strands were 100% complementary thereby confirming the high accuracy of the determined sequence. The *tuf* sequences determined using the above strategy are all in the Sequence Listing (i.e. SEQ ID NOs: 118 to 146). Table 13 gives the originating microbial species and the source for 30 each *tuf* sequence in the Sequence Listing.

The alignment of the *tuf* sequences determined by us or selected from databases reveals clearly that the length of the sequenced portion of the *tuf* genes is variable. There may be insertions or deletions of several amino acids. This explains why the size of the sequenced *tuf* amplification product was variable for both bacterial 35 and fungal species. Among the *tuf* sequences determined by our group, we found insertions and deletions adding up to 5 amino acids or 15 nucleotides. Consequently, the nucleotide positions indicated on top of each of Annexes I to V do not correspond for *tuf* sequences having insertions or deletions.

It should also be noted that the various *tuf* sequences determined by us

occasionally contain degenerescences. These degenerated nucleotides correspond to sequence variations between *tufA* and *tufB* genes because the amplification primers amplify both *tuf* genes. These nucleotide variations were not attributable to nucleotide misincorporations by the *taq* DNA polymerase because the sequence of both strands 5 were identical and also because the sequences determined with both preparations of the gel-purified *tuf* amplicons were identical.

**The selection of amplification primers from *tuf* sequences**

The *tuf* sequences determined by us or selected from databases were used to select PCR primers for (i) the universal detection of bacteria, (ii) the genus-specific 10 detection and identification of *Enterococcus* spp. and *Staphylococcus* spp. and (iii) the species-specific detection and identification of *Candida albicans*. The strategy used to select these PCR primers was based on the analysis of multiple sequence alignments of various *tuf* sequences. For more details about the selection of PCR primers from *tuf* sequences, please refer to Examples 1 to 3 and Annexes I to IV.

15 **The selection of amplification primers from *recA***

The comparison of the nucleotide sequence for the *recA* gene from various bacterial species including 5 species of streptococci allowed the selection of *Streptococcus*-specific PCR primers. For more details about the selection of PCR primers from *recA*, please refer to Example 4 and Annex V.

20 **DNA fragment isolation from *Staphylococcus saprophyticus* by arbitrarily primed PCR**

DNA sequences of unknown coding potential for the species-specific detection and identification of *Staphylococcus saprophyticus* were obtained by the method of arbitrarily primed PCR (AP-PCR).

25 AP-PCR is a method which can be used to generate specific DNA probes for microorganisms (Fani *et al.*, 1993, *Mol. Ecol.* 2:243-250). A description of the AP-PCR protocol used to isolate a species-specific genomic DNA fragment from *Staphylococcus saprophyticus* follows. Twenty different oligonucleotide primers of 10 nucleotides in length (all included in the AP-PCR kit OPAD (Operon Technologies, Inc., 30 Alameda, CA)) were tested systematically with DNAs from 3 bacterial strains of *Staphylococcus saprophyticus* (all obtained from the American Type Culture Collection (ATCC): numbers 15305, 35552 and 43867) as well as with DNA from four other staphylococcal species (*Staphylococcus aureus* ATCC 25923, *Staphylococcus epidermidis* ATCC 14990, *Staphylococcus haemolyticus* ATCC 29970 and 35 *Staphylococcus hominis* ATCC 35982). For all bacterial species, amplification was performed from a bacterial suspension adjusted to a standard 0.5 McFarland which corresponds to approximately  $1.5 \times 10^8$  bacteria/mL. One  $\mu$ L of the standardized bacterial suspension was transferred directly to 19  $\mu$ L of a PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl<sub>2</sub>,

1.2  $\mu$ M of only one of the 20 different AP-PCR primers OPAD, 200  $\mu$ M of each of the four dNTPs and 0.5 unit of *Taq* DNA polymerase (Promega Corp., Madison, WI). PCR reactions were subjected to cycling using a MJ Research PTC-200 thermal cycler (MJ Research Inc.) as follows: 3 min at 96°C followed by 35 cycles of 1 min at 95°C for the 5 denaturation step, 1 min at 32°C for the annealing step and 1 min at 72°C for the extension step. A final extension step of 7 min at 72°C was made after the 35 cycles to ensure complete extension of PCR products. Subsequently, twenty microliters of the 10 PCR amplified mixture were resolved by electrophoresis in a 2% agarose gel containing 0.25  $\mu$ g/mL of ethidium bromide. The size of the amplification products was estimated by comparison with a 50-bp molecular weight ladder.

Amplification patterns specific for *Staphylococcus saprophyticus* were observed with the AP-PCR primer OPAD-9 (SEQ ID NO: 25). Amplification with this primer consistently showed a band corresponding to a DNA fragment of approximately 450 bp for all *Staphylococcus saprophyticus* strains tested but not for any of the four other 15 staphylococcal species tested. This species-specific pattern was confirmed by testing 10 more clinical isolates of *S. saprophyticus* selected from the culture collection of the microbiology laboratory of the CHUL as well as strains selected from the gram-positive bacterial species listed in Table 5.

The band corresponding to the approximately 450 bp amplicon which was 20 specific and ubiquitous for *S. saprophyticus* based on AP-PCR was excised from the agarose gel and purified using the QIAquick™ gel extraction kit (QIAGEN Inc.). The gel-purified DNA fragment was cloned into the T/A cloning site of the pCR 2.1™ plasmid vector (Invitrogen Inc.) using T4 DNA ligase (New England BioLabs). Recombinant plasmids were transformed into *E. coli* DH5 $\alpha$  competent cells using 25 standard procedures. Plasmid DNA isolation was done by the method of Birnboim and Doly (Nucleic Acids Res. 7:1513-1523) for small-scale preparations. All plasmid DNA preparations were digested with the *Eco*RI restriction endonuclease to ensure the presence of the approximately 450 bp AP-PCR insert into the recombinant plasmids. Subsequently, a large-scale and highly purified plasmid DNA preparation was 30 performed from two selected clones shown to carry the AP-PCR insert by using the QIAGEN plasmid purification kit. These plasmid preparations were used for automated DNA sequencing.

Both strands of the AP-PCR insert from the two selected clones were 35 sequenced by the dideoxynucleotide chain termination sequencing method with SP6 and T7 sequencing primers, by using an Applied Biosystems automated DNA sequencer as described previously. The analysis of the obtained sequences revealed that the DNA sequences for both strands from each clone were 100% complementary. Furthermore, it showed that the entire sequence determined for each clone were both identical. These sequencing data confirm the 100% accuracy for the determined 438

bp sequence (SEQ ID NO: 29). Optimal amplification primers have been selected from the sequenced AP-PCR *Staphylococcus saprophyticus* DNA fragment with the help of the primer analysis software Oligo™ 4.0. The selected primer sequences have been tested in PCR assays to verify their specificity and ubiquity (Table 7). These PCR 5 primers were specific since there was no amplification with DNA from bacterial species other than *S. saprophyticus* selected from Tables 4 and 5. Furthermore, this assay was ubiquitous since 245 of 260 strains of *S. saprophyticus* were efficiently amplified with this PCR assay. When used in combination with another *S. saprophyticus*-specific 10 PCR assay, which is an object of our co-pending U.S. (N.S. 08/526,840) and PCT (PCT/CA/95/00528) patent applications, the ubiquity reaches 100% for these 260 strains.

#### DNA amplification

For DNA amplification by the widely used PCR (polymerase chain reaction) 15 method, primer pairs were derived from proprietary DNA fragments or from database sequences. Prior to synthesis, the potential primer pairs were analyzed by using the Oligo™ 4.0 software to verify that they are good candidates for PCR amplification.

During DNA amplification by PCR, two oligonucleotide primers binding 20 respectively to each strand of the heat-denatured target DNA from the bacterial genome are used to amplify exponentially *in vitro* the target DNA by successive thermal cycles allowing denaturation of the DNA, annealing of the primers and synthesis of new targets at each cycle (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.).

Briefly, the PCR protocols were as follow: Treated clinical specimens or 25 standardized bacterial or fungal suspensions (see below) were amplified in a 20 µL PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 2.5 mM MgCl<sub>2</sub>, 0.4 µM of each primer, 200 µM of each of the four dNTPs and 0.5 unit of *Taq* DNA polymerase (Promega) combined with the TaqStart™ antibody (Clontech Laboratories Inc., Palo Alto, CA). The TaqStart™ antibody, which is a neutralizing monoclonal 30 antibody to *Taq* DNA polymerase, was added to all PCR reactions to enhance the specificity and the sensitivity of the amplifications (Kellogg *et al.*, 1994, Biotechniques 16:1134-1137). The treatment of the clinical specimens varies with the type of specimen tested, since the composition and the sensitivity level required are different for each specimen type. It consists in a rapid protocol to lyse the bacterial cells and 35 eliminate the PCR inhibitory effects (see example 11 for urine specimen preparation). For amplification from bacterial or fungal cultures, the samples were added directly to the PCR amplification mixture without any pre-treatment step (see example 10). Primer sequences derived from highly conserved regions of the bacterial 16S ribosomal RNA gene were used to provide an internal control for all PCR reactions. Alternatively, the

internal control was derived from sequences not found in microorganisms or in the human genome. The internal control was integrated into all amplification reactions to verify the efficiency of the PCR assays and to ensure that significant PCR inhibition was absent. The internal control derived from rRNA was also useful to monitor the efficiency of bacterial lysis protocols.

PCR reactions were then subjected to thermal cycling (3 min at 95°C followed by 30 cycles of 1 second at 95°C for the denaturation step and 30 second at 55°C for the annealing-extension step) using a PTC-200 thermal cycler (MJ Research Inc.) and subsequently analyzed by standard ethidium bromide-stained agarose gel electrophoresis. The number of cycles performed for the PCR assays varies according to the sensitivity level required. For example, the sensitivity level required for microbial detection directly from clinical specimens is higher for blood specimens than for urine specimens because the concentration of microorganisms associated with a septicemia can be much lower than that associated with a urinary tract infection. Consequently, more sensitive PCR assays having more thermal cycles are required for direct detection from blood specimens. Similarly, PCR assays performed directly from bacterial or fungal cultures may be less sensitive than PCR assays performed directly from clinical specimens because the number of target organisms is normally much lower in clinical specimens than in microbial cultures.

It is clear that other methods for the detection of specific amplification products, which may be faster and more practical for routine diagnosis, may be used. Such methods may be based on the detection of fluorescence after amplification (e.g. TaqMan™ system from Perkin Elmer or Amplisensor™ from Biotronics). Methods based on the detection of fluorescence are particularly promising for utilization in routine diagnosis as they are very rapid, quantitative and can be automated (Example 14).

Microbial pathogens detection and identification may also be performed by solid support or liquid hybridization using species-specific internal DNA probes hybridizing to an amplification product. Such probes may be generated from any species-specific or genus-specific DNA amplification products which are objects of the present invention. Alternatively, the internal probes for species or genus detection and identification may be derived from the amplicons produced by the universal amplification assay. The oligonucleotide probes may be labeled with biotin or with digoxigenin or with any other reporter molecules.

To assure PCR efficiency, glycerol, dimethyl sulfoxide (DMSO) or other related solvents can be used to increase the sensitivity of the PCR and to overcome problems associated with the amplification of a target DNA having a high GC content or forming strong secondary structures (Dieffenbach and Dveksler, 1995, PCR Primer : A Laboratory Manual, Cold Spring Harbor Laboratory Press, Plainview, New York). The

concentration ranges for glycerol and DMSO are 5-15% (v/v) and 3-10% (v/v), respectively. For the PCR reaction mixture, the concentration ranges for the amplification primers and MgCl<sub>2</sub> are 0.1-1.5 μM and 1.5-3.5 mM, respectively. Modifications of the standard PCR protocol using external and nested primers (i.e. 5 nested PCR) or using more than one primer pair (i.e. multiplex PCR) may also be used (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.). For more details about the PCR protocols and amplicon detection methods, see Examples 9 to 14.

10 The person skilled in the art of DNA amplification knows the existence of other rapid amplification procedures such as ligase chain reaction (LCR), transcription-mediated amplification (TMA), self-sustained sequence replication (3SR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA), branched DNA (bDNA) and cycling probe technology (CPT) (Lee *et al.*, 1997, Nucleic Acid Amplification Technologies: Application to Disease Diagnosis, Eaton Publishing, 15 Boston, MA ; Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.). The scope of this invention is not limited to the use of amplification by PCR, but rather includes the use of any rapid nucleic acid amplification method or any other procedure which may be used to increase rapidity and sensitivity of the tests. Any oligonucleotide suitable for 20 the amplification of nucleic acids by approaches other than PCR and derived from the species-specific, genus-specific and universal DNA fragments as well as from selected antibiotic resistance gene sequences included in this document are also under the scope of this invention.

#### Hybridization assays with oligonucleotide probes

25 In hybridization experiments, single-stranded oligonucleotides (size less than 100 nucleotides) have some advantages over DNA fragment probes for the detection of bacteria, such as ease of synthesis in large quantities, consistency in results from batch to batch and chemical stability. Briefly, for the hybridizations, oligonucleotides were 5' end-labeled with the radionucleotide  $\gamma$ -<sup>32</sup>P(dATP) using T4 polynucleotide 30 kinase (Pharmacia) (Sambrook *et al.*, 1989, Molecular Cloning: A Laboratory Manual, 2<sup>nd</sup> ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). The unincorporated radionucleotide was removed by passing the labeled oligonucleotide through a Sephadex G-50™ column. Alternatively, oligonucleotides were labeled with biotin, either enzymatically at their 3' ends or incorporated directly during synthesis at 35 their 5' ends, or with digoxigenin. It will be appreciated by the person skilled in the art that labeling means other than the three above labels may be used.

Each oligonucleotide probe was then tested for its specificity by hybridization to DNAs from a variety of bacterial and fungal species selected from Tables 4, 5 and 6. All of the bacterial or fungal species tested were likely to be pathogens associated

with common infections or potential contaminants which can be isolated from clinical specimens. Each target DNA was released from bacterial cells using standard chemical treatments to lyse the cells (Sambrook *et al.*, 1989, Molecular Cloning: A Laboratory Manual, 2<sup>nd</sup> ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). Subsequently, the DNA was denatured by conventional methods and then irreversibly fixed onto a solid support (e.g. nylon or nitrocellulose membranes) or free in solution. The fixed single-stranded target DNAs were then hybridized with the oligonucleotide probe cells (Sambrook *et al.*, 1989, Molecular Cloning: A Laboratory Manual, 2<sup>nd</sup> ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). Pre-hybridization conditions were in 1 M NaCl + 10% dextran sulfate + 1% SDS + 100 µg/mL salmon sperm DNA at 65°C for 15 min. Hybridization was performed in fresh pre-hybridization solution containing the labeled probe at 65°C overnight. Post-hybridization washing conditions were as follows: twice in 3X SSC containing 1% SDS, twice in 2X SSC containing 1% SDS and twice in 1X SSC containing 1% SDS (all of these washes were at 65°C for 15 min), and a final wash in 0.1X SSC containing 1% SDS at 25°C for 15 min. Autoradiography of washed filters allowed the detection of selectively hybridized probes. Hybridization of the probe to a specific target DNA indicated a high degree of similarity between the nucleotide sequence of these two DNAs because of the high stringency of the washes.

An oligonucleotide probe was considered specific only when it hybridized solely to DNA from the species or genus from which it was isolated. Oligonucleotide probes found to be specific were subsequently tested for their ubiquity (i.e. ubiquitous probes recognized most or all isolates of the target species or genus) by hybridization to microbial DNAs from clinical isolates of the species or genus of interest including ATCC strains. The DNAs from strains of the target species or genus were denatured, fixed onto nylon membranes and hybridized as described above. Probes were considered ubiquitous when they hybridized specifically with the DNA from at least 80% of the isolates of the target species or genus.

**Specificity and ubiquity tests for oligonucleotide primers and probes**

The specificity of oligonucleotide primers and probes, derived either from the DNA fragments sequenced by us or selected from databases, was tested by amplification of DNA or by hybridization with bacterial or fungal species selected from those listed in Tables 4, 5 and 6, as described in the two previous sections. Oligonucleotides found to be specific were subsequently tested for their ubiquity by amplification (for primers) or by hybridization (for probes) with bacterial DNAs from isolates of the target species or genus. Results for specificity and ubiquity tests with the oligonucleotide primers are summarized in Table 7. The specificity and ubiquity of the PCR assays using the selected amplification primer pairs were tested directly from cultures (see Examples 9 and 10) of bacterial or fungal species.

The various species-specific and genus-specific PCR assays which are objects of the present invention are all specific. For the PCR assays specific to bacterial species or genus, this means that DNA isolated from a wide variety of bacterial species, other than that from the target species or genus and selected from Tables 4 and 5, could not be amplified. For the PCR assay specific to *Candida albicans*, it means there was no amplification with genomic DNA from the fungal species listed in Table 6 as well as with a variety of bacterial species selected from Tables 4 and 5.

The various species-specific and genus-specific PCR assays which are objects of the present invention are also all ubiquitous (Table 7). (i) The species-specific PCR assays for *E. faecium*, *L. monocytogenes*, *S. saprophyticus*, *S. agalactiae* and *C. albicans* amplified genomic DNA from all or most strains of the target species tested, which were obtained from various sources and which are representative of the diversity within each target species (Table 7). The species identification of all of these strains was based on classical biochemical methods which are routinely used in clinical microbiology laboratories. (ii) The genus-specific PCR assays specific for *Enterococcus* spp., *Staphylococcus* spp., *Streptococcus* spp. and *Neisseria* spp. amplified genomic DNA from all or most strains of the target genus tested, which represent all clinically important bacterial species for each target genus. These strains were obtained from various sources and are representative of the diversity within each target genus. Again, the species identification of all of these strains was based on classical biochemical methods which are routinely used in clinical microbiology laboratories. More specifically, the four genus-specific PCR assays amplified the following species: (1) The *Enterococcus*-specific assay amplified efficiently DNA from all of the 11 enterococcal species tested including *E. avium*, *E. casseliflavus*, *E. dispar*, *E. durans*, *E. faecalis*, *E. faecium*, *E. flavescentis*, *E. gallinarum*, *E. hirae*, *E. mundtii* and *E. raffinosus*. (2) The *Neisseria*-specific assay amplified efficiently DNA from all of the 12 neisserial species tested including *N. canis*, *N. cinerea*, *N. elongata*, *N. flavaescens*, *N. gonorrhoeae*, *N. lactamica*, *N. meningitidis*, *N. mucosa*, *N. polysaccharea*, *N. sicca*, *N. subflava* and *N. weaveri*. (3) The *Staphylococcus*-specific assay amplified efficiently DNA from 13 of the 14 staphylococcal species tested including *S. aureus*, *S. auricularis*, *S. capitis*, *S. cohnii*, *S. epidermidis*, *S. haemolyticus*, *S. hominis*, *S. lugdunensis*, *S. saprophyticus*, *S. schleiferi*, *S. simulans*, *S. warneri* and *S. xylosus*. The staphylococcal species which could not be amplified is *S. sciuri*. (4) Finally, the *Streptococcus*-specific assay amplified efficiently DNA from all of the 22 streptococcal species tested including *S. agalactiae*, *S. anginosus*, *S. bovis*, *S. constellatus*, *S. crista*, *S. dysgalactiae*, *S. equi*, *S. gordonii*, *S. intermedius*, *S. mitis*, *S. mutans*, *S. oralis*, *S. parasanguis*, *S. pneumoniae*, *S. pyogenes*, *S. salivarius*, *S. sanguis*, *S. sabrinus*, *S. suis*, *S. uberis*, *S. vestibularis* and *S. viridans*. On the other hand, the *Streptococcus*-specific assay did not amplify 3 out of 9 strains

of *S. mutans* and 1 out of 23 strains of *S. salivarius*, thereby showing a slight lack of ubiquity for these two streptococcal species.

All specific and ubiquitous amplification primers for each target microbial species or genus or antibiotic resistance gene investigated are listed in Annex VI.

5 Divergence in the sequenced DNA fragments can occur, insofar as the divergence of these sequences or a part thereof does not affect the specificity of the probes or amplification primers. Variant bacterial DNA is under the scope of this invention.

The PCR amplification primers listed in Annex VI were all tested for their specificity and ubiquity using reference strains as well as clinical isolates from various 10 geographical locations. The 351 reference strains used to test the amplification and hybridization assays (Tables 4, 5 and 6) were obtained from (i) the American Type Culture Collection (ATCC): 85%, (ii) the Laboratoire de santé publique du Québec (LSPQ): 10%, (iii) the Centers for Disease Control and Prevention (CDC): 3% , (iv) the National Culture Type Collection (NCTC): 1% and (v) several other reference 15 laboratories throughout the world: 1%. These reference strains are representative of (i) 90 gram-negative bacterial species (169 strains; Table 4), (ii) 97 gram-positive bacterial species (154 strains; Table 5) and (iii) 12 fungal species (28 strains; Table 6).

#### Antibiotic resistance genes

Antimicrobial resistance complicates treatment and often leads to therapeutic 20 failures. Furthermore, overuse of antibiotics inevitably leads to the emergence of bacterial resistance. Our goal is to provide clinicians, in approximately one hour, the needed information to prescribe optimal treatments. Besides the rapid identification of negative clinical specimens with DNA-based tests for universal bacterial detection and the identification of the presence of a specific pathogen in the positive specimens with 25 species- and/or genus-specific DNA-based tests, clinicians also need timely information about the ability of the bacterial pathogen to resist antibiotic treatments. We feel that the most efficient strategy to evaluate rapidly bacterial resistance to antimicrobials is to detect directly from the clinical specimens the most common and clinically important antibiotic resistance genes (i.e. DNA-based tests for the detection 30 of antibiotic resistance genes). Since the sequence from the most important and common bacterial antibiotic resistance genes are available from databases, our strategy was to use the sequence from a portion or from the entire resistance gene to design specific oligonucleotide primers or probes which will be used as a basis for the development of rapid DNA-based tests. The sequence from each of the bacterial 35 antibiotic resistance genes selected on the basis of their clinical relevance (i.e. high incidence and importance) is given in the Sequence Listing. Tables 9 and 10 summarize some characteristics of the selected antibiotic resistance genes. Our approach is unique because the antibiotic resistance genes detection and the bacterial detection and identification are performed simultaneously in multiplex assays under

uniform PCR amplification conditions (Example 13).

Annex VI provides a list of all amplification primers selected from 26 clinically important antibiotic resistance genes which were tested in PCR assays. The various PCR assays for antibiotic resistance genes detection and identification were validated 5 by testing several resistant bacterial isolates known to carry the targeted gene and obtained from various countries. The testing of a large number of strains which do not carry the targeted resistance gene was also performed to ensure that all assays were specific. So far, all PCR assays for antibiotic resistance genes are highly specific and have detected all control resistant bacterial strains known to carry the targeted gene. 10 The results of some clinical studies to validate the array of PCR assays for the detection and identification of antibiotic resistance genes and correlate these DNA-based assays with standard antimicrobials susceptibility testing methods are presented in Tables 11 and 12.

#### Universal bacterial detection

15 In the routine microbiology laboratory, a high percentage of clinical specimens sent for bacterial identification are negative by culture (Table 4). Testing clinical samples with universal amplification primers or universal probes to detect the presence of bacteria prior to specific identification and screen out the numerous negative specimens is thus useful as it saves costs and may rapidly orient the clinical 20 management of the patients. Several amplification primers and probes were therefore synthesized from highly conserved portions of bacterial sequences from the *tuf* genes (Table 8). The universal primer selection was based on a multiple sequence alignment constructed with sequences determined by us or selected from available database sequences as described in Example 1 and Annex I.

25 For the identification of database sequences suitable for the universal detection of bacteria, we took advantage of the fact that the complete genome sequences for two distant microorganisms (i.e. *Mycoplasma genitalium* and *Haemophilus influenzae*) are available. A comparison of the amino acid sequence for all proteins encoded by the genome of these two distant microorganisms led to the identification of highly 30 homologous proteins. An analysis of these homologous proteins allowed to select some promising candidates for the development of universal DNA-based assays for the detection of bacteria. Since the complete nucleotide sequence of several other microbial genomes are presently available in databases, a person skilled in the art could arrive to the same conclusions by comparing genomes sequences other than 35 those of *Mycoplasma genitalium* and *Haemophilus influenzae*. The selected *tuf* gene encodes a protein (EF-Tu) involved in the translation process during protein synthesis. Subsequently, an extensive nucleotide sequence analysis was performed with the *tuf* gene sequences available in databases as well as with novel *tuf* sequences which we have determined as described previously. All computer analysis of amino acid and

nucleotide sequences were performed by using the GCG programs. Subsequently, optimal PCR primers for the universal amplification of bacteria were selected with the help of the Oligo™ program. The selected primers are degenerated at several nucleotide positions and contain several inosines in order to allow the amplification of 5 all clinically relevant bacterial species (Annex I). Inosine is a nucleotide analog able to specifically bind to any of the four nucleotides A, C, G or T. Degenerated oligonucleotides consist of an oligonucleotide mix having two or more of the four nucleotides A, C, G or T at the site of mismatches. The inclusion of inosine and/or of 10 degenerescences in the amplification primers allow mismatch tolerance thereby permitting the amplification of a wider array of target nucleotide sequences (Dieffenbach and Dveksler, 1995 PCR Primer: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Plainview, NY).

The amplification conditions with the universal primers were identical to those used for the species- and genus-specific amplification assays except that the 15 annealing temperature was 50°C instead of 55°C. This universal PCR assay was specific and nearly ubiquitous for the detection of bacteria. The specificity for bacteria was verified by amplifying genomic DNA isolated from the 12 fungal species listed in Table 6 as well as genomic DNA from *Leishmania donovani*, *Saccharomyces cerevisiae* and human lymphocytes. None of the above eukaryotic DNA preparations 20 could be amplified by the universal assay, thereby suggesting that this test is specific for bacteria. The ubiquity of the universal assay was verified by amplifying genomic DNAs from 116 reference strains which represent 95 of the most clinically relevant bacterial species. These species have been selected from the bacterial species listed in Tables 4 and 5. We found that 104 of these 116 strains could be amplified. The 25 bacterial species which could not be amplified belong to the following genera: *Corynebacterium* (11 species) and *Stenotrophomonas* (1 species). Sequencing of the *tuf* genes from these bacterial species has been recently performed. This sequencing data has been used to select new universal primers which may be more ubiquitous. These primers are in the process of being tested. We also observed that for several 30 species the annealing temperature had to be reduced to 45°C in order to get an efficient amplification. These bacterial species include *Gemella morbillum*, *Listeria* spp. (3 species) and *Gardnerella vaginalis*. It is important to note that the 95 bacterial species selected from Tables 4 and 5 to test the ubiquity of the universal assay include all of the most clinically relevant bacterial species associated with a variety of human 35 infections acquired in the community or in hospitals (nosocomial infections). The most clinically important bacterial and fungal pathogens are listed in Tables 1 and 2.

## EXAMPLES AND ANNEXES

The following examples and annexes are intended to be illustrative of the various methods and compounds of the invention, rather than limiting the scope thereof.

5 The various annexes show the strategies used for the selection of amplification primers from *tuf* sequences or from the *recA* gene: (i) Annex I illustrates the strategy used for the selection of the universal amplification primers from *tuf* sequences. (ii) Annex II shows the strategy used for the selection of the amplification primers specific for the genus *Enterococcus* from *tuf* sequences. (iii) Annex III illustrates the strategy 10 used for the selection of the amplification primers specific for the genus *Staphylococcus* from *tuf* sequences. (iv) Annex IV shows the strategy used for the selection of the amplification primers specific for the species *Candida albicans* from *tuf* sequences. (v) Annex V illustrates the strategy used for the selection of the amplification primers specific for the genus *Streptococcus* from *recA* sequences. (vi) 15 Annex VI gives a list of all selected primer pairs. As shown in these annexes, the selected amplification primers may contain inosines and/or degenerescences. Inosine is a nucleotide analog able to specifically bind to any of the four nucleotides A, C, G or T. Alternatively, degenerated oligonucleotides which consist of an oligonucleotide mix having two or more of the four nucleotides A, C, G or T at the site of mismatches 20 were used. The inclusion of inosine and/or of degenerescences in the amplification primers allow mismatch tolerance thereby permitting the amplification of a wider array of target nucleotide sequences (Dieffenbach and Dveksler, 1995 PCR Primer: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Plainview, New York).

## EXAMPLES

### 25 EXAMPLE 1 :

Selection of universal PCR primers from *tuf* sequences. As shown in Annex I, the comparison of *tuf* sequences from a variety of bacterial and eukaryotic species allowed the selection of PCR primers which are universal for the detection of bacteria. The strategy used to design the PCR primers was based on the analysis of a multiple 30 sequence alignment of various *tuf* sequences. This multiple sequence alignment includes *tuf* sequences from 38 bacterial species and 3 eukaryotic species either determined by us or selected from databases (Table 13). A careful analysis of this multiple sequence alignment allowed the selection of primer sequences which are conserved within eubacteria but which discriminate sequences from eukaryotes, 35 thereby permitting the universal detection of bacteria. As shown in Annex I, the selected primers contain several inosines and degenerescences. This was necessary because there is a relatively high polymorphism among bacterial *tuf* sequences despite the fact that this gene is highly conserved. In fact, among the *tuf* sequences that we determined, we found many nucleotide variations as well as some deletions and/or

insertions of amino acids. The selected universal primers were specific and ubiquitous for bacteria (Table 7). Of the 95 most clinically important bacterial species tested, 12 were not amplified. These species belong to the genera *Corynebacterium* (11 species) and *Stenotrophomonas* (1 species). The universal primers did not amplify DNA of non-bacterial origin, including human and other types of eukaryotic DNA.

5 **EXAMPLE 2 :**

10 Selection of genus-specific PCR primers from *tuf* sequences. As shown in Annexes 2 and 3, the comparison of *tuf* sequences from a variety of bacterial species allowed the selection of PCR primers specific for *Enterococcus* spp. or for *Staphylococcus* spp. The strategy used to design the PCR primers was based on the analysis of a multiple sequence alignment of various *tuf* sequences. These multiple sequence alignments include the *tuf* sequences of four representative bacterial species selected from each target genus as well as *tuf* sequences from species of other closely related bacterial genera. A careful analysis of those alignments allowed the selection 15 of oligonucleotide sequences which are conserved within the target genus but which discriminate sequences from other closely related genera, thereby permitting the genus-specific and ubiquitous detection and identification of the target bacterial genus.

20 For the selection of primers specific for *Enterococcus* spp. (Annex II), we have sequenced a portion of approximately 890 bp of the *tuf* genes for *Enterococcus avium*, *E. faecalis*, *E. faecium* and *E. gallinarum*. All other *tuf* sequences used in the alignment were either sequenced by us or selected from databases. The analysis of this sequence alignment led to the selection of a primer pair specific and ubiquitous for *Enterococcus* spp. (Table 7). All of the 11 enterococcal species tested were efficiently 25 amplified and there was no amplification with genomic DNA from bacterial species of other genera.

30 For the selection of primers specific for *Staphylococcus* spp. (Annex III), we have also sequenced a portion of approximately 890 bp of the *tuf* genes for *Staphylococcus aureus*, *S. epidermidis*, *S. saprophyticus* and *S. simulans*. All other *tuf* sequences used in the alignment were either sequenced by us or selected from databases. The analysis of this sequence alignment led to the selection of two primer pairs specific and ubiquitous for *Staphylococcus* spp. (Table 7). Annex III shows the strategy used to select one of these two PCR primer pairs. The same strategy was used to select the other primer pair. Of the 14 staphylococcal species tested, one (*S. sciuri*) could not be amplified by the *Staphylococcus*-specific PCR assays using either 35 one of these two primer pairs. For PCR assays using either one of these two primer pairs, there was no amplification with DNA from species of other bacterial genera.

**EXAMPLE 3 :**

Selection from *tuf* sequences of PCR primers specific for *Candida albicans*. As shown in Annex IV, the comparison of *tuf* sequences from a variety of bacterial and eukaryotic species allowed the selection of PCR primers specific for *Candida albicans*.

5 The strategy used to design the PCR primers was based on the analysis of a multiple sequence alignment of various *tuf* sequences. This multiple sequence alignment includes *tuf* sequences of five representative fungal species selected from the genus *Candida* which were determined by our group (i.e. *C. albicans*, *C. glabrata*, *C. krusei*, *C. parapsilosis* and *C. tropicalis*) as well as *tuf* sequences from other closely related

10 fungal species. *tuf* sequences from various bacterial species were also included. A careful analysis of this sequence alignment allowed the selection of primers from the *C. albicans* *tuf* sequence; these primers discriminate sequences from other closely related *Candida* species and other fungal species, thereby permitting the species-specific and ubiquitous detection and identification of *C. albicans* (Table 7). All of 88

15 *Candida albicans* strains tested were efficiently amplified and there was no amplification with genomic DNA from other fungal or bacterial species.

**EXAMPLE 4:**

Selection of PCR primers specific for *Streptococcus* from *recA*. As shown in Annex V, the comparison of the various bacterial *recA* gene sequences available from databases (GenBank and EMBL) was used as a basis for the selection of PCR primers which are specific and ubiquitous for the bacterial genus *Streptococcus*. Since sequences of the *recA* gene are available for many bacterial species including five species of streptococci, it was possible to choose sequences well conserved within the genus *Streptococcus* but distinct from the *recA* sequences for other bacterial genera.

25 When there were mismatches between the *recA* gene sequences from the five *Streptococcus* species, an inosine residue was incorporated into the primer (Annex V). The selected primers, each containing one inosine and no degenerescence, were specific and ubiquitous for *Streptococcus* species (Table 7). This PCR assay amplified all of the 22 streptococcal species tested. However, the *Streptococcus*-specific assay

30 did not amplify DNA from 3 out of 9 strains of *S. mutans* and 1 out of 3 strains of *S. salivarius*. There was no amplification with genomic DNA from other bacterial genera (Table 7).

**EXAMPLE 5:**

Nucleotide sequencing of DNA fragments. The nucleotide sequence of a portion of the *tuf* genes from a variety of bacterial or fungal species was determined by using the dideoxynucleotide chain termination sequencing method (Sanger *et al.*, 1977, Proc. Natl. Acad. Sci. USA. 74:5463-5467). The sequencing was performed by using an Applied Biosystems automated DNA sequencer (model 373A) with their PRISM™ Sequenase® Terminator Double-stranded DNA Sequencing Kit (Perkin-Elmer Corp.,

Applied Biosystems Division, Foster City, CA). The sequencing strategy does not discriminate *tufA* and *tufB* genes because the sequencing primers hybridize efficiently to both bacterial *tuf* genes. These DNA sequences are shown in the sequence listing (SEQ ID Nos: 118 to 146). The presence of several degenerated nucleotides in the 5 various *tuf* sequences determined by our group (Table 13) corresponds to sequence variations between *tufA* and *tufB*.

10 Oligonucleotide primers and probes selection. Oligonucleotide probes and amplification primers were selected from the given proprietary DNA fragments or database sequences using the Oligo™ program and were synthesized with an automated ABI DNA synthesizer (Model 391, Perkin-Elmer Corp., Applied Biosystems Division) using phosphoramidite chemistry.

**EXAMPLE 6 :**

15 Labeling of oligonucleotides for hybridization assays. Each oligonucleotide was 5' end-labeled with  $\gamma$ -<sup>32</sup>P (dATP) by the T4 polynucleotide kinase (Pharmacia) as described earlier. The label could also be non-radioactive.

20 Specificity test for oligonucleotide probes. All labeled oligonucleotide probes were tested for their specificity by hybridization to DNAs from a variety of bacterial and fungal species selected from Tables 4, 5 and 6 as described earlier. Species-specific or genus-specific probes were those hybridizing only to DNA from the microbial 25 species or genus from which it was isolated. Oligonucleotide probes found to be specific were submitted to ubiquity tests as follows.

30 Ubiquity test for oligonucleotide probes. Specific oligonucleotide probes were then used in ubiquity tests with strains of the target species or genus including reference strains and other strains obtained from various countries and which are representative of the diversity within each target species or genus. Chromosomal DNAs from the isolates were transferred onto nylon membranes and hybridized with labeled oligonucleotide probes as described for specificity tests. The batteries of isolates constructed for each target species or genus contain reference ATCC strains as well as a variety of clinical isolates obtained from various sources. Ubiquitous probes were those hybridizing to at least 80% of DNAs from the battery of clinical isolates of the target species or genus.

**EXAMPLE 7:**

35 Same as example 6 except that a pool of specific oligonucleotide probes is used for microbial identification (i) to increase sensitivity and assure 100% ubiquity or (ii) to identify simultaneously more than one microbial species and/or genus. Microbial identification could be performed from microbial cultures or directly from any clinical specimen.

**EXAMPLE 8:**

5 Same as example 6 except that bacteria or fungi were detected directly from clinical samples. Any biological sample was loaded directly onto a dot blot apparatus and cells were lysed *in situ* for bacterial or fungal detection and identification. Blood samples should be heparinized in order to avoid coagulation interfering with their convenient loading on a dot blot apparatus.

**EXAMPLE 9:**

10 PCR amplification. The technique of PCR was used to increase the sensitivity and the rapidity of the assays. The sets of primers were tested in PCR assays performed directly from bacterial colonies or from a standardized bacterial suspension (see Example 10) to determine their specificity and ubiquity (Table 7). Examples of 15 specific and ubiquitous PCR primer pairs are listed in Annex VI.

15 Specificity and ubiquity tests for amplification primers. The specificity of all selected PCR primer pairs was tested against DNAs from a variety of bacterial and fungal species selected from Tables 4, 5 and 6 as described earlier. Primer pairs found specific for each species or genus were then tested for their ubiquity to ensure that each set of primers could amplify at least 90% of DNAs from a battery of isolates of the target species or genus. The batteries of isolates constructed for each species contain 20 reference ATCC strains and various clinical isolates from around the world which are representative of the diversity within each species or genus.

Standard precautions to avoid false positive PCR results should be taken (Kwok and Higuchi, 1989, *Nature*, 239:237-238). Methods to inactivate PCR amplification products such as the inactivation by uracil-N-glycosylase may be used to control PCR carryover.

**25 EXAMPLE 10:**

30 Amplification directly from bacterial or yeast cultures. PCR assays were performed either directly from a bacterial colony or from a bacterial suspension, the latter being adjusted to a standard McFarland 0.5 (corresponds to approximately  $1.5 \times 10^8$  bacteria/mL). In the case of direct amplification from a colony, a portion of a colony was transferred using a plastic rod directly into a 20  $\mu$ L PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl<sub>2</sub>, 0.4  $\mu$ M of each primer, 200  $\mu$ M of each of the four dNTPs and 0.5 unit of *Taq* DNA polymerase (Promega) combined with the *TaqStart*™ antibody (Clontech Laboratories Inc.). For the bacterial suspension, 1  $\mu$ L of the cell suspension was added to 19  $\mu$ L of the same PCR reaction mixture. For the identification from yeast cultures, 1  $\mu$ L of a standard McFarland 1.0 (corresponds to approximately  $3.0 \times 10^8$  bacteria/mL) concentrated 100 times by centrifugation was added directly to the PCR reaction. This concentration step for yeast cells was performed because a McFarland 0.5 for yeast cells has approximately 200 times fewer cells than a McFarland 0.5 for bacterial cells.

PCR reactions were then subjected to thermal cycling (3 min at 95°C followed by 30 cycles of 1 second at 95°C for the denaturation step and 30 seconds at 55°C for the annealing-extension step) using a PTC-200 thermal cycler. PCR amplification products were then analyzed by standard agarose gel (2%) electrophoresis.

5 Amplification products were visualized in agarose gels containing 0.25 µg/mL of ethidium bromide under UV at 254 nm. The entire PCR assay can be completed in approximately one hour.

Primer sequences derived from highly conserved regions of the bacterial 16S ribosomal RNA gene were used to provide an internal control for all PCR reactions.

10 Alternatively, the internal control was derived from sequences not found in microorganisms or in the human genome. The internal control was integrated into all amplification reactions to verify the efficiency of the PCR assays and to ensure that significant PCR inhibition was absent. The internal control derived from rRNA was also useful to monitor the efficiency of the bacterial lysis protocols. The internal control and

15 the species-specific or genus-specific amplifications were performed simultaneously in multiplex PCR assays.

**EXAMPLE 11:**

Amplification directly from urine specimens. For PCR amplification performed directly from urine specimens, 1 µL of urine was mixed with 4 µL of a lysis solution containing 500 mM KCl, 100 mM tris-HCl (pH 9.0), 1% triton X-100. After incubation for at least 15 minutes at room temperature, 1 µL of the treated urine specimen was added directly to 19 µL of the PCR reaction mixture. The final concentration of the PCR reagents was 50 mM KCl, 10 mM Tris (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl<sub>2</sub>, 0.4 µM of each primer, 200 µM of each of the four dNTPs. In addition, each 20 µL reaction contained 0.5 unit of *Taq* DNA polymerase (Promega) combined with the *TaqStart*™ antibody (Clontech Laboratories Inc.).

Strategies for the internal control, PCR amplification and agarose gel detection of the amplicons are as previously described in example 10.

**EXAMPLE 12:**

Detection of antibiotic resistance genes. The presence of specific antibiotic resistance genes which are frequently encountered and clinically relevant is identified using the PCR amplification or hybridization protocols described previously. Specific oligonucleotides used as a basis for the DNA-based tests are selected from the antibiotic resistance gene sequences. These tests, which allow the rapid evaluation of bacterial resistance to antimicrobial agents, can be performed either directly from clinical specimens, from a standardized bacterial suspension or from a bacterial colony and should complement diagnostic tests for the universal detection of bacteria as well as for the species-specific and genus-specific microbial detection and identification.

**EXAMPLE 13:**

Same as examples 10 and 11 except that assays were performed by multiplex PCR (i.e. using several pairs of primers in a single PCR reaction) to reach an ubiquity of 100% for the specific targeted pathogen(s). For more heterogeneous microbial species or genus, a combination of PCR primer pairs may be required to detect and identify all representatives of the target species or genus.

10 Multiplex PCR assays could also be used to (i) detect simultaneously several microbial species and/or genera or, alternatively, (ii) to simultaneously detect and identify bacterial and/or fungal pathogens and detect specific antibiotic resistance genes either directly from a clinical specimen or from bacterial cultures.

15 For these applications, amplicon detection methods should be adapted to differentiate the various amplicons produced. Standard agarose gel electrophoresis could be used because it discriminates the amplicons based on their sizes. Another useful strategy for this purpose would be detection using a variety of fluorescent dyes emitting at different wavelengths. The fluorescent dyes can be each coupled with a specific oligonucleotide linked to a fluorescence quencher which is degraded during amplification to release the fluorescent dyes (e.g. TaqMan™, Perkin Elmer).

**EXAMPLE 14:**

20 Detection of amplification products. The person skilled in the art will appreciate that alternatives other than standard agarose gel electrophoresis (Example 10) may be used for the revelation of amplification products. Such methods may be based on fluorescence polarization or on the detection of fluorescence after amplification (e.g. Amplisensor™, Biotronics; TaqMan™, Perkin-Elmer Corp.) or other labels such as biotin (SHARP Signal™ system, Digene Diagnostics). These methods are quantitative 25 and may be automated. One of the amplification primers or an internal oligonucleotide probe specific to the amplicon(s) derived from the species-specific, genus-specific or universal DNA fragments is coupled with the fluorescent dyes or with any other label. Methods based on the detection of fluorescence are particularly suitable for diagnostic tests since they are rapid and flexible as fluorescent dyes emitting at different 30 wavelengths are available.

**EXAMPLE 15:**

35 Species-specific, genus-specific, universal and antibiotic resistance gene amplification primers can be used in other rapid amplification procedures such as the ligase chain reaction (LCR), transcription-mediated amplification (TMA), self-sustained sequence replication (3SR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA), cycling probe technology (CPT) and branched DNA (bDNA) or any other methods to increase the sensitivity of the test. Amplifications can be performed from isolated bacterial cultures or directly from any clinical specimen. The scope of this invention is therefore not limited to the use of the

DNA sequences from the enclosed Sequence Listing for PCR only but rather includes the use of any procedures to specifically detect bacterial DNA and which may be used to increase rapidity and sensitivity of the tests.

**EXAMPLE 16:**

5        A test kit would contain sets of probes specific for each microbial species or genus as well as a set of universal probes. The kit is provided in the form of test components, consisting of the set of universal probes labeled with non-radioactive labels as well as labeled species- or genus-specific probes for the detection of each pathogen of interest in specific types of clinical samples. The kit will also include test 10 reagents necessary to perform the pre-hybridization, hybridization, washing steps and hybrid detection. Finally, test components for the detection of known antibiotic resistance genes (or derivatives therefrom) will be included. Of course, the kit will include standard samples to be used as negative and positive controls for each hybridization test.

15       Components to be included in the kits will be adapted to each specimen type and to detect pathogens commonly encountered in that type of specimen. Reagents for the universal detection of bacteria will also be included. Based on the sites of infection, the following kits for the specific detection of pathogens may be developed:

20       - A kit for the universal detection of bacterial or fungal pathogens from all clinical specimens which contains sets of probes specific for highly conserved regions of the microbial genomes.

25       - A kit for the detection of microbial pathogens retrieved from urine samples, which contains 5 specific test components (sets of probes for the detection of *Enterococcus faecium*, *Enteroccus* species, *Staphylococcus saprophyticus*, *Staphylococcus* species and *Candida albicans*).

30       - A kit for the detection of respiratory pathogens which contains 3 specific test components (sets of probes for the detection of *Staphylococcus* species, *Enterococcus* species and *Candida albicans*).

35       - A kit for the detection of pathogens retrieved from blood samples, which contains 10 specific test components (sets of probes for the detection of *Streptococcus* species, *Streptococcus agalactiae*, *Staphylococcus* species, *Staphylococcus saprophyticus*, *Enterococcus* species, *Enterococcus faecium*, *Neisseria* species, *Neisseria meningitidis*, *Listeria monocytogenes* and *Candida albicans*). This kit can also be applied for direct detection and identification from blood cultures.

          - A kit for the detection of pathogens causing meningitis, which contains 5 specific test components (sets of probes for the detection of *Streptococcus* species, *Listeria monocytogenes*, *Neisseria meningitidis*, *Neisseria* species and *Staphylococcus* species).

5 - A kit for the detection of clinically important antibiotic resistance genes which contains sets of probes for the specific detection of at least one of the 26 following genes associated with antibiotic resistance: *bla<sub>tem</sub>*, *bla<sub>rob</sub>*, *bla<sub>shv</sub>*, *bla<sub>oxa</sub>*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aacA4*, *aac6'-Ila*, *ermA*, *ermB*, *ermC*, *mecA*, *vanA*, *vanB*, *vanC*, *satA*, *aac(6')-aph(2")*, *aad(6')*, *vat*, *vga*, *msrA*, *sul* and *int*.

10 - Other kits adapted for the detection of pathogens from skin, abdominal wound or any other clinically relevant infections may also be developed.

**EXAMPLE 17:**

15 Same as example 16 except that the test kits contain all reagents and controls to perform DNA amplification assays. Diagnostic kits will be adapted for amplification by PCR (or other amplification methods) performed directly either from clinical specimens or from microbial cultures. Components required for (i) universal bacterial detection, (ii) species-specific and genus-specific bacterial and/or fungal detection and identification and (iii) detection of antibiotic resistance genes will be included.

20 25 Amplification assays could be performed either in tubes or in microtitration plates having multiple wells. For assays in plates, the wells will contain the specific amplification primers and control DNAs and the detection of amplification products will be automated. Reagents and amplification primers for universal bacterial detection will be included in kits for tests performed directly from clinical specimens. Components required for species-specific and genus-specific bacterial and/or fungal detection and identification as well as for the simultaneous antibiotic resistance genes detection will be included in kits for testing directly from bacterial or fungal cultures as well as in kits for testing directly from any type of clinical specimen.

30 The kits will be adapted for use with each type of specimen as described in example 16 for hybridization-based diagnostic kits.

**EXAMPLE 18:**

35 It is understood that the use of the probes and amplification primers described in this invention for bacterial and/or fungal detection and identification is not limited to clinical microbiology applications. In fact, we feel that other sectors could also benefit from these new technologies. For example, these tests could be used by industries for quality control of food, water, air, pharmaceutical products or other products requiring microbiological control. These tests could also be applied to detect and identify bacteria or fungi in biological samples from organisms other than humans (e.g. other primates, birds, plants, mammals, farm animals, livestock and others). These diagnostic tools could also be very useful for research purposes including clinical trials and epidemiological studies.

This invention has been described herein above, and it is readily apparent that modifications can be made thereto without departing from the spirit of this invention. These modifications are under the scope of this invention, as defined in the appended claims.

**Table 1. Distribution (%) of nosocomial pathogens for various human infections in USA (1990-1992)<sup>1</sup>.**

	Pathogen	UTI <sup>2</sup>	SSI <sup>3</sup>	BSI <sup>4</sup>	Pneumonia	CSF <sup>5</sup>
5	<i>Escherichia coli</i>	27	9	5	4	2
	<i>Staphylococcus aureus</i>	2	21	17	21	2
	<i>Staphylococcus epidermidis</i>	2	6	20	0	1
	<i>Enterococcus faecalis</i>	16	12	9	2	0
	<i>Enterococcus faecium</i>	1	1	0	0	0
10	<i>Pseudomonas aeruginosa</i>	12	9	3	18	0
	<i>Klebsiella pneumoniae</i>	7	3	4	9	0
	<i>Proteus mirabilis</i>	5	3	1	2	0
	<i>Streptococcus pneumoniae</i>	0	0	3	1	18
	Group B <i>Streptococci</i>	1	1	2	1	6
15	Other <i>Streptococci</i>	3	5	2	1	3
	<i>Haemophilus influenzae</i>	0	0	0	6	45
	<i>Neisseria meningitidis</i>	0	0	0	0	14
	<i>Listeria monocytogenes</i>	0	0	0	0	3
	Other <i>Enterococci</i>	1	1	0	0	0
20	Other <i>Staphylococci</i>	2		8	13	20
	<i>Candida albicans</i>	9	3	5	5	0
	Other <i>Candida</i>	2		1	3	10
	<i>Enterobacter</i> spp.	5	7	4	12	2
	<i>Acinetobacter</i> spp.	1	1	2	4	2
25	<i>Citrobacter</i> spp.	2	1	1	1	0
	<i>Serratia marcescens</i>	1	1	1	3	1
	Other <i>Klebsiella</i>	1	1	1	2	1
	Others	0	6	4	5	0

30 <sup>1</sup> Data recorded by the National Nosocomial Infections Surveillance (NNIS) from 80 hospitals (Emori and Gaynes, 1993, Clin. Microbiol. Rev., 6:428-442).

<sup>2</sup> Urinary tract infection.

<sup>3</sup> Surgical site infection.

<sup>4</sup> Bloodstream infection.

35 <sup>5</sup> Cerebrospinal fluid.

**Table 2. Distribution (%) of bloodstream infection pathogens in Quebec (1995), Canada (1992), UK (1969-1988) and USA (1990-1992).**

5	Organism	Quebec <sup>1</sup>	Canada <sup>2</sup>	UK <sup>3</sup>		USA <sup>4</sup>
				Community-acquired	Hospital-acquired	
	<i>E. coli</i>	15.6	53.8	24.8	20.3	5.0
	<i>S. epidermidis</i>	25.8	NI <sup>6</sup>	0.5	7.2	31.0
	and other CoNS <sup>5</sup>					
10	<i>S. aureus</i>	9.6	NI	9.7	19.4	16.0
	<i>S. pneumoniae</i>	6.3	NI	22.5	2.2	NR <sup>7</sup>
	<i>E. faecalis</i>	3.0	NI	1.0	4.2	NR
	<i>E. faecium</i>	2.6	NI	0.2	0.5	NR
	<i>Enterococcus</i> spp.	NR	NI	NR	NR	9.0
15	<i>H. influenzae</i>	1.5	NR	3.4	0.4	NR
	<i>P. aeruginosa</i>	1.5	8.2	1.0	8.2	3.0
	<i>K. pneumoniae</i>	3.0	11.2	3.0	9.2	4.0
	<i>P. mirabilis</i>	NR	3.9	2.8	5.3	1.0
20	<i>S. pyogenes</i>	NR	NI	1.9	0.9	NR
	<i>Enterobacter</i> spp.	4.1	5.5	0.5	2.3	4.0
	<i>Candida</i> spp.	8.5	NI	NR	1.0	8.0
	Others	18.5	17.4 <sup>8</sup>	28.7	18.9	19.0

25 <sup>1</sup> Data obtained for 270 isolates collected at the Centre Hospitalier de l'Université Laval (CHUL) during a 5 month period (May to October 1995).

<sup>2</sup> Data from 10 hospitals throughout Canada representing 941 gram-negative bacterial isolates. (Chamberland *et al.*, 1992, Clin. Infect. Dis., 15:615-628).

<sup>3</sup> Data from a 20-year study (1969-1988) for nearly 4000 isolates (Eykyn *et al.*, 1990, J. Antimicrob. Chemother., Suppl. C, 25:41-58).

<sup>4</sup> Data recorded by the National Nosocomial Infections Surveillance (NNIS) from 80 hospitals (Emori and Gaynes, 1993, Clin. Microbiol. Rev., 6:428-442).

<sup>5</sup> Coagulase-negative staphylococci.

<sup>6</sup> NI, not included. This survey included only gram-negative species.

35 <sup>7</sup> NR, incidence not reported for these species or genera.

<sup>8</sup> In this case, 17.4 stands for other gram-negative bacterial species.

**Table 3. Distribution of positive and negative clinical specimens tested at the microbiology laboratory of the CHUL (February 1994 – January 1995).**

	Clinical specimens and/or sites	No. of samples tested (%)	% of positive specimens	% of negative specimens
5	Urine	17,981 (54.5)	19.4	80.6
	Blood culture/marrow	10,010 (30.4)	6.9	93.1
	Sputum	1,266 (3.8)	68.4	31.6
	Superficial pus	1,136 (3.5)	72.3	27.7
10	Cerebrospinal fluid	553 (1.7)	1.0	99.0
	Synovial fluid	523 (1.6)	2.7	97.3
	Respiratory tract	502 (1.5)	56.6	43.4
	Deep pus	473 (1.4)	56.8	43.2
	Ears	289 (0.9)	47.1	52.9
15	Pleural and pericardial fluid	132 (0.4)	1.0	99.0
	Peritoneal fluid	101(0.3)	28.6	71.4
	<b>Total:</b>	<b>32,966 (100.0)</b>	<b>20.0</b>	<b>80.0</b>

**Table 4. Gram-negative bacterial species (90) used to test the specificity of PCR primers and DNA probes (continues on next page).**

	Bacterial species	Number of reference strains tested <sup>a</sup>	Bacterial species	Number of reference strains tested <sup>a</sup>
5	<i>Acinetobacter baumannii</i>	1	<i>Moraxella phenylpyruvica</i>	1
	<i>Acinetobacter lwoffii</i>	3	<i>Morganella morganii</i>	1
	<i>Actinobacillus lignieresii</i>	1	<i>Neisseria animalis</i>	1
	<i>Alcaligenes faecalis</i>	1	<i>Neisseria canis</i>	1
	<i>Alcaligenes odorans</i>	1	<i>Neisseria caviae</i>	1
10	<i>Alcaligenes xylosoxydans</i>		<i>Neisseria cinerea</i>	1
	subsp. <i>denitrificans</i>	1	<i>Neisseria cuniculi</i>	1
	<i>Bacteroides distasonis</i>	1	<i>Neisseria elongata</i>	1
			subsp. <i>elongata</i>	
	<i>Bacteroides fragilis</i>	1	<i>Neisseria elongata</i>	1
			subsp. <i>glycoytica</i>	
	<i>Bacteroides ovatus</i>	1	<i>Neisseria flavescens</i>	1
15	<i>Bacteroides</i>	1	<i>Neisseria flavescens</i>	1
	<i>thetaiotaomicron</i>		<i>Branham</i>	
	<i>Bacteroides vulgatus</i>	1	<i>Neisseria gonorrhoeae</i>	18
	<i>Bordetella bronchiseptica</i>	1	<i>Neisseria lactamica</i>	1
	<i>Bordetella parapertussis</i>	1	<i>Neisseria meningitidis</i>	4
20	<i>Bordetella pertussis</i>	2	<i>Neisseria mucosa</i>	2
	<i>Burkholderia cepacia</i>	1	<i>Neisseria polysaccharea</i>	1
	<i>Citrobacter amalonaticus</i>	1	<i>Neisseria sicca</i>	3
	<i>Citrobacter diversus</i>	2	<i>Neisseria subflava</i>	3
	subsp. <i>koseri</i>			
25	<i>Citrobacter freundii</i>	1	<i>Neisseria weaveri</i>	1
	<i>Comamonas acidovorans</i>	1	<i>Ochrobactrum antropi</i>	1
	<i>Enterobacter aerogenes</i>	1	<i>Pasteurella aerogenes</i>	1
	<i>Enterobacter</i>	1	<i>Pasteurella multocida</i>	1
	<i>agglomerans</i>			
30	<i>Enterobacter cloacae</i>	1	<i>Prevotella melaninogenica</i>	1
	<i>Escherichia coli</i>	9	<i>Proteus mirabilis</i>	3
	<i>Escherichia fergusonii</i>	1	<i>Proteus vulgaris</i>	1

	Bacterial species	Number of reference strains tested <sup>a</sup>	Bacterial species	Number of reference strains tested <sup>a</sup>
	<i>Escherichia hermannii</i>	1	<i>Providencia alcalifaciens</i>	1
	<i>Escherichia vulneris</i>	1	<i>Providencia rettgeri</i>	1
	<i>Flavobacterium meningosepticum</i>	1	<i>Providencia rustigianii</i>	1
5	<i>Flavobacterium indologenes</i>	1	<i>Providencia stuartii</i>	1
	<i>Flavobacterium odoratum</i>	1	<i>Pseudomonas aeruginosa</i>	14
	<i>Fusobacterium necrophorum</i>	2	<i>Pseudomonas fluorescens</i>	2
10	<i>Gardnerella vaginalis</i>	1	<i>Pseudomonas stutzeri</i>	1
	<i>Haemophilus haemolyticus</i>	1	<i>Salmonella arizona</i>	1
	<i>Haemophilus influenzae</i>	12	<i>Salmonella choleraesuis</i>	1
	<i>Haemophilus parahaemolyticus</i>	1	<i>Salmonella gallinarum</i>	1
15	<i>Haemophilus parainfluenzae</i>	2	<i>Salmonella typhimurium</i>	3
	<i>Hafnia alvei</i>	1	<i>Serratia liquefaciens</i>	1
	<i>Kingella indologenes</i>	1	<i>Serratia marcescens</i>	1
20	subsp. <i>suttonella</i>			
	<i>Kingella kingae</i>	1	<i>Shewanella putida</i>	1
	<i>Klebsiella ornithinolytica</i>	1	<i>Shigella boydii</i>	1
	<i>Klebsiella oxytoca</i>	1	<i>Shigella dysenteriae</i>	1
	<i>Klebsiella pneumoniae</i>	8	<i>Shigella flexneri</i>	1
25	<i>Moraxella atlantae</i>	1	<i>Shigella sonnei</i>	1
	<i>Moraxella catarrhalis</i>	5	<i>Stenotrophomonas maltophilia</i>	1
	<i>Moraxella lacunata</i>	1	<i>Yersinia enterocolitica</i>	1
	<i>Moraxella osloensis</i>	1		

30 <sup>a</sup> Most reference strains were obtained from the American Type Culture Collection (ATCC). The other reference strains were obtained from (i) the Laboratoire de Santé Publique du Québec (LSPQ), (ii) the Center for Disease Control and Prevention (CDC) and (iii) the National Culture Type Collection (NCTC).

**Table 5. Gram-positive bacterial species (97) used to test the specificity of PCR primers and DNA probes (continues on next page).**

	Bacterial species	Number of reference strains tested <sup>a</sup>	Bacterial species	Number of reference strains tested <sup>a</sup>
5	<i>Abiotrophia adiacens</i>	1	<i>Micrococcus kristinae</i>	1
	<i>Abiotrophia defectiva</i>	1	<i>Micrococcus luteus</i>	1
	<i>Actinomyces israelii</i>	1	<i>Micrococcus lylae</i>	1
	<i>Clostridium perfringens</i>	1	<i>Micrococcus roseus</i>	1
	<i>Corynebacterium accolens</i>	1	<i>Micrococcus varians</i>	1
10	<i>Corynebacterium aquaticum</i>	1	<i>Peptococcus niger</i>	1
	<i>Corynebacterium bovis</i>	1	<i>Peptostreptococcus anaerobius</i>	1
	<i>Corynebacterium cervicis</i>	1	<i>Peptostreptococcus asaccharolyticus</i>	1
	<i>Corynebacterium diphtheriae</i>	6	<i>Staphylococcus aureus</i>	10
15	<i>Corynebacterium flavescentis</i>	1	<i>Staphylococcus auricularis</i>	1
	<i>Corynebacterium genitalium</i>	6	<i>Staphylococcus capitis</i> subsp. <i>urealyticus</i>	1
	<i>Corynebacterium jeikeium</i>	1	<i>Staphylococcus cohnii</i>	1
20	<i>Corynebacterium kutcheri</i>	1	<i>Staphylococcus epidermidis</i>	2
	<i>Corynebacterium matruchotii</i>	1	<i>Staphylococcus haemolyticus</i>	2
	<i>Corynebacterium minutissimum</i>	1	<i>Staphylococcus hominis</i>	2
	<i>Corynebacterium mycetoides</i>	1	<i>Staphylococcus lugdunensis</i>	1
25	<i>Corynebacterium pseudodiphtheriticum</i>	1	<i>Staphylococcus saprophyticus</i>	3
	<i>Corynebacterium pseudogenitalium</i>	6	<i>Staphylococcus schleiferi</i>	1
	<i>Corynebacterium renale</i>	1	<i>Staphylococcus sciuri</i>	1
30	<i>Corynebacterium striatum</i>	1	<i>Staphylococcus simulans</i>	1
	<i>Corynebacterium ulcerans</i>	1	<i>Staphylococcus warneri</i>	1

	Bacterial species	Number of reference strains tested <sup>a</sup>	Bacterial species	Number of reference strains tested <sup>a</sup>
	<i>Corynebacterium urealyticum</i>	1	<i>Staphylococcus xylosus</i>	1
	<i>Corynebacterium xerosis</i>	1	<i>Streptococcus agalactiae</i>	6
	<i>Enterococcus avium</i>	1	<i>Streptococcus anginosus</i>	2
5	<i>Enterococcus casseliflavus</i>	1	<i>Streptococcus bovis</i>	2
	<i>Enterococcus cecorum</i>	1	<i>Streptococcus constellatus</i>	1
	<i>Enterococcus dispar</i>	1	<i>Streptococcus crista</i>	1
	<i>Enterococcus durans</i>	1	<i>Streptococcus dysgalactiae</i>	1
10	<i>Enterococcus faecalis</i>	6	<i>Streptococcus equi</i>	1
	<i>Enterococcus faecium</i>	3	<i>Streptococcus gordonii</i>	1
	<i>Enterococcus flavescentis</i>	1	Group C Streptococci	1
	<i>Enterococcus gallinarum</i>	3	Group D Streptococci	1
	<i>Enterococcus hirae</i>	1	Group E Streptococci	1
15	<i>Enterococcus mundtii</i>	1	Group F Streptococci	1
	<i>Enterococcus pseudoavium</i>	1	Group G Streptococci	1
	<i>Enterococcus raffinosus</i>	1	<i>Streptococcus intermedius</i>	1
	<i>Enterococcus</i>	1	<i>Streptococcus mitis</i>	2
20	<i>saccharolyticus</i>			
	<i>Enterococcus solitarius</i>	1	<i>Streptococcus mutans</i>	1
	<i>Eubacterium lentum</i>	1	<i>Streptococcus oralis</i>	1
	<i>Gemella haemolysans</i>	1	<i>Streptococcus parasanguis</i>	1
	<i>Gemella morbillorum</i>	1	<i>Streptococcus pneumoniae</i>	6
25	<i>Lactobacillus acidophilus</i>	1	<i>Streptococcus pyogenes</i>	3
	<i>Listeria innocua</i>	1	<i>Streptococcus salivarius</i>	2
	<i>Listeria ivanovii</i>	1	<i>Streptococcus sanguis</i>	2
	<i>Listeria grayi</i>	1	<i>Streptococcus sobrinus</i>	1
	<i>Listeria monocytogenes</i>	3	<i>Streptococcus suis</i>	1
30	<i>Listeria murrayi</i>	1	<i>Streptococcus uberis</i>	1
	<i>Listeria seeligeri</i>	1	<i>Streptococcus vestibularis</i>	1
	<i>Listeria welshimeri</i>	1		

<sup>a</sup> Most reference strains were obtained from the American Type Culture Collection (ATCC). The other reference strains were obtained from (i) the Laboratoire de Santé Publique du Québec (LSPQ), (ii) the Center for Disease Control and Prevention (CDC) and (iii) the National Culture Type Collection (NCTC).

**Table 6. Fungal species (12) used to test the specificity of PCR primers and DNA probes.**

	Fungal species	Number of reference strains tested <sup>a</sup>
5	<i>Candida albicans</i>	12
	<i>Candida glabrata</i>	1
	<i>Candida guilliermondii</i>	1
	<i>Candida kefyr</i>	3
10	<i>Candida krusei</i>	2
	<i>Candida lusitaniae</i>	1
	<i>Candida parapsilosis</i>	2
	<i>Candida tropicalis</i>	3
	<i>Rhodotorula glutinis</i>	1
15	<i>Rhodotorula minuta</i>	1
	<i>Rhodotorula rubra</i>	1
	<i>Saccharomyces cerevisiae</i>	1

<sup>a</sup> Most reference strains were obtained from (i) the American Type Culture Collection (ATCC) and (ii) the Laboratoire de Santé Publique du Québec (LSPQ).

**Table 7. PCR assays developed for several clinically important bacterial and fungal pathogens (continues on next page).**

	Organism	Primer Pair <sup>a</sup> SEQ ID NO	Amplicon size (bp)	Ubiquity <sup>b</sup>	DNA amplification from	
					culture <sup>c</sup>	specimens <sup>d</sup>
	<i>Enterococcus faecium</i>	1-2	216	79/80	+	+
5	<i>Listeria monocytogenes</i>	3-4	130	164/168 <sup>e</sup>	+	+
	<i>Neisseria meningitidis</i>	5-6	177	258/258	+	+
	<i>Staphylococcus saprophyticus</i>	7-8	149	245/260	+	NT
10	<i>Streptococcus agalactiae</i>	9-10	154	29/29	+	+
	<i>Candida albicans</i>	11-12	149	88/88	+	NT
	<i>Enterococcus</i> spp. (11 species) <sup>f</sup>	13-14	112	87/87	+	NT
	<i>Neisseria</i> spp.	15-16	103	321/321	+	+
15	(12 species) <sup>f</sup>					
	<i>Staphylococcus</i> spp.	17-18	192	13/14	+	NT
	(14 species)					
		19-20	221	13/14	+	NT
	<i>Streptococcus</i> spp.	21-22	153	210/214 <sup>g</sup>	+	+
20	(22 species) <sup>f</sup>					
	Universal detection <sup>h</sup>	23-24	309	104/ 116 <sup>i</sup>	+	+
	(95 species) <sup>j</sup>					

<sup>a</sup> All primer pairs are specific in PCR assays since no amplification was observed with DNA from the bacterial and fungal species other than the species of interest listed in Tables 4, 5 and 6.

<sup>b</sup> Ubiquity was tested by using reference strains as well as strains from throughout the world, which are representative of the diversity within each target species or genus.

<sup>c</sup> For all primer pairs, PCR amplifications performed directly from a standardized microbial suspension (MacFarland) or from a colony were all specific and ubiquitous.

<sup>d</sup> PCR assays performed directly from blood cultures, urine specimens or

cerebrospinal fluid. NT, not tested.

- The four *L. monocytogenes* strains undetected are not clinical isolates. These strains were isolated from food and are not associated with a human infection.
- 5     • The bacterial species tested include all those clinically relevant for each genus (Tables 4 and 5). All of these species were efficiently amplified by their respective genus-specific PCR assay, except for the *Staphylococcus*-specific assay, which does not amplify *S. sciuri*.
- 9     • The *Streptococcus*-specific PCR assay did not amplify 3 out of 9 strains of *S. mutans* and 1 out of 3 strains of *S. salivarius*.
- 10    • The primers selected for universal bacterial detection do not amplify DNA of non-bacterial origin, including human and other types of eukaryotic genomic DNA.
- 15    • For the universal amplification, the 95 bacterial species tested represent the most clinically important bacterial species listed in Tables 4 and 5. The 12 strains not amplified are representatives of genera *Corynebacterium* (11 species) and *Stenotrophomonas* (1 species).

**Table 8. Target genes for the various genus-specific, species-specific and universal amplification assays.**

	Microorganisms	Gene	Protein encoded
20	<i>Candida albicans</i>	<i>tuf</i>	translation elongation factor EF-Tu
	<i>Enterococcus faecium</i>	<i>ddl</i>	D-alanine:D-alanine ligase
	<i>Listeria monocytogenes</i>	<i>actA</i>	actin-assembly inducing protein
	<i>Neisseria meningitidis</i>	<i>omp</i>	outer membrane protein
25	<i>Streptococcus agalactiae</i>	<i>cAMP</i>	cAMP factor
	<i>Staphylococcus saprophyticus</i>	unknown	unknown
	<i>Enterococcus</i> spp.	<i>tuf</i>	translation elongation factor EF-Tu
	<i>Neisseria</i> spp.	<i>asd</i>	ASA-dehydrogenase
30	<i>Staphylococcus</i> spp.	<i>tuf</i>	translation elongation factor EF-Tu
	<i>Streptococcus</i> spp.	<i>recA</i>	RecA protein
	Universal detection	<i>tuf</i>	translation elongation factor EF-Tu

**Table 9. Antibiotic resistance genes selected for diagnostic purposes.**

Genes	SEQ ID NOs		Antibiotics	Bacteria <sup>a</sup>
	selected primers	originating fragment		
5	<i>bla<sub>oxb</sub></i>	49-50	110	β-lactams
	<i>blaZ</i>	51-52	111	β-lactams
	<i>aac6'-Ila</i>	61-64	112	Aminoglycosides
	<i>ermA</i>	91-92	113	Macrolides
	<i>ermB</i>	93-94	114	Macrolides
	<i>ermC</i>	95-96	115	Macrolides
	<i>vanB</i>	71-74	116	Vancomycin
10	<i>vanC</i>	75-76	117	Vancomycin
	<i>aad(6')</i>	173-174	-	Streptomycin
15				<i>Enterococcus</i> spp.

<sup>a</sup> Bacteria having high incidence for the specified antibiotic resistance genes. The presence of these antibiotic resistance genes in other bacteria is not excluded.

**Table 10. Antibiotic resistance genes from our co-pending US (N.S. 08/526840) and PCT (PCT/CA/95/00528) patent applications for which we have selected PCR primer pairs.**

5	Genes	SEQ ID NOs of selected primers	Antibiotics	Bacteria <sup>a</sup>
	<i>bla<sub>tem</sub></i>	37-40	β-lactams	<i>Enterobacteriaceae</i> , <i>Pseudomonadaceae</i> , <i>Haemophilus</i> spp., <i>Neisseria</i> spp.
10	<i>bla<sub>rob</sub></i>	45-48	β-lactams	<i>Haemophilus</i> spp., <i>Pasteurella</i> spp.
	<i>bla<sub>shv</sub></i>	41-44	β-lactams	<i>Klebsiella</i> spp. and other
	<i>aadB</i>	53-54	Aminoglycosides	<i>Enterobacteriaceae</i>
	<i>aacC1</i>	55-56		<i>Pseudomonadaceae</i>
	<i>aacC2</i>	57-58		
15	<i>aacC3</i>	59-60		
	<i>aacA4</i>	65-66		
	<i>mecA</i>	97-98	β-lactams	<i>Staphylococcus</i> spp.
	<i>vanA</i>	67-70	Vancomycin	<i>Enterococcus</i> spp.
	<i>satA</i>	81-82	Macrolides	<i>Enterococcus</i> spp.
20	<i>aac(6')-aph(2")</i>	83-86	Aminoglycosides	<i>Enterococcus</i> spp., <i>Staphylococcus</i> spp.
	<i>vat</i>	87-88	Macrolides	<i>Staphylococcus</i> spp.
	<i>vga</i>	89-90	Macrolides	<i>Staphylococcus</i> spp.
	<i>msrA</i>	77-80	Erythromycin	<i>Staphylococcus</i> spp.
	<i>int</i>	99-102	β-lactams, trimethoprim,	<i>Enterobacteriaceae</i> ,
25	<i>sul</i>	103-106	aminoglycosides, antiseptic, chloramphenicol	<i>Pseudomonadaceae</i>

<sup>a</sup> Bacteria having high incidence for the specified antibiotic resistance genes. The presence of these antibiotic resistance genes in other bacteria is not excluded.

**Table 11. Correlation between disk diffusion and PCR amplification of antibiotic resistance genes in *Staphylococcus* species<sup>a</sup>.**

5	Antibiotic	Phenotype	PCR	Disk diffusion (Kirby-Bauer) <sup>b</sup>		
				Resistant	Intermediate	Sensitive
10	Penicillin	<i>blaZ</i>	+	165	0	0
			-	0	0	31
15	Oxacillin	<i>mecA</i>	+	51	11	4
			-	2	0	128
20	Gentamycin	<i>aac(6')aph(2")</i>	+	24	18	6
			-	0	0	148
25	Erythromycin	<i>ermA</i>	+	15	0	0
		<i>ermB</i>	+	0	0	0
		<i>ermC</i>	+	43	0	0
30		<i>msrA</i>	+	4	0	0
			-	0	1	136

<sup>a</sup> The *Staphylococcus* strains studied include *S. aureus* (82 strains), *S. epidermidis* (83 strains), *S. hominis* (2 strains), *S. capitis* (3 strains), *S. haemolyticus* (9 strains), *S. simulans* (12 strains) and *S. warneri* (5 strains), for a total of 196 strains.

<sup>b</sup> Susceptibility testing was performed by the method of Kirby-Bauer according to the protocol recommended by the National Committee of Clinical Laboratory Standards (NCCLS).

**Table 12. Correlation between disk diffusion profiles and PCR amplification of antibiotic resistance genes in *Enterococcus* species<sup>a</sup>.**

	Antibiotic	Phenotype	PCR	Disk diffusion (Kirby-Bauer) <sup>b</sup>	
				Resistant	Sensitive
5		<i>blaZ</i>	+	0	2
	Ampicillin		-	1	30
				51	1
	Gentamycin	<i>aac(6')aph(2")</i>	+	3	38
10	Streptomycin	<i>aad(6')</i>	+	26	15
			-	6	27
	Vancomycin	<i>vanA</i>	+	36	0
		<i>vanB</i>	+	26	0
15			-	0	40

<sup>a</sup> The *Enterococcus* strains studied include *E. faecalis* (33 strains) and *E. faecium* (69 strains), for a total of 102 strains.

<sup>b</sup> Susceptibility testing was performed by the method of Kirby-Bauer according to the protocol recommended by the National Committee of Clinical Laboratory Standards (NCCLS).

**Table 13. Origin of *tuf* sequences in the Sequence Listing (continues on next page).**

	SEQ ID NO	Bacterial or fungal species	Source
5	118	<i>Abiotrophia adiacens</i>	This patent
	119	<i>Abiotrophia defectiva</i>	This patent
	120	<i>Candida albicans</i>	This patent
	121	<i>Candida glabrata</i>	This patent
	122	<i>Candida krusei</i>	This patent
10	123	<i>Candida parapsilosis</i>	This patent
	124	<i>Candida tropicalis</i>	This patent
	125	<i>Corynebacterium accolens</i>	This patent
	126	<i>Corynebacterium diphtheriae</i>	This patent
	127	<i>Corynebacterium genitalium</i>	This patent
15	128	<i>Corynebacterium jeikeium</i>	This patent
	129	<i>Corynebacterium pseudotuberculosis</i>	This patent
	130	<i>Corynebacterium striatum</i>	This patent
	131	<i>Enterococcus avium</i>	This patent
	132	<i>Enterococcus faecalis</i>	This patent
20	133	<i>Enterococcus faecium</i>	This patent
	134	<i>Enterococcus gallinarum</i>	This patent
	135	<i>Gardnerella vaginalis</i>	This patent
	136	<i>Listeria innocua</i>	This patent
	137	<i>Listeria ivanovii</i>	This patent
25	138	<i>Listeria monocytogenes</i>	This patent
	139	<i>Listeria seeligeri</i>	This patent
	140	<i>Staphylococcus aureus</i>	This patent
	141	<i>Staphylococcus epidermidis</i>	This patent
	142	<i>Staphylococcus saprophyticus</i>	This patent
30	143	<i>Staphylococcus simulans</i>	This patent
	144	<i>Streptococcus agalactiae</i>	This patent
	145	<i>Streptococcus pneumoniae</i>	This patent

SEQ ID NO	Bacterial or fungal species	Source
146	<i>Streptococcus salivarius</i>	This patent
147	<i>Agrobacterium tumefaciens</i>	Database
148	<i>Bacillus subtilis</i>	Database
149	<i>Bacteroides fragilis</i>	Database
5	150 <i>Borrelia burgdorferi</i>	Database
	151 <i>Brevibacterium linens</i>	Database
	152 <i>Burkholderia cepacia</i>	Database
	153 <i>Chlamydia trachomatis</i>	Database
	154 <i>Escherichia coli</i>	Database
10	155 <i>Fibrobacter succinogenes</i>	Database
	156 <i>Flavobacterium ferrugineum</i>	Database
	157 <i>Haemophilus influenzae</i>	Database
	158 <i>Helicobacter pylori</i>	Database
	159 <i>Micrococcus luteus</i>	Database
15	160 <i>Mycobacterium tuberculosis</i>	Database
	161 <i>Mycoplasma genitalium</i>	Database
	162 <i>Neisseria gonorrhoeae</i>	Database
	163 <i>Rickettsia prowazekii</i>	Database
	164 <i>Salmonella typhimurium</i>	Database
20	165 <i>Shewanella putida</i>	Database
	166 <i>Stigmatella aurantiaca</i>	Database
	167 <i>Streptococcus pyogenes</i>	Database
	168 <i>Thiobacillus cuprinus</i>	Database
	169 <i>Treponema pallidum</i>	Database
25	170 <i>Ureaplasma urealyticum</i>	Database
	171 <i>Wolinella succinogenes</i>	Database

Annex I: Strategy for the selection from *tuf* sequences of the universal amplification primers (continues on pages 49 to 51).

		SEQ ID
491	517...776	802
5 Abiotrophia adiacens	<u>CAACTGTAAC</u> <u>TGGTGTGAA</u> ATGTTCC...AA <u>ATGGT</u> AATGCC <u>TGGT</u> GATAAC <u>GTAA</u>	NO 118
Abiotrophia defectiva	CTACCGTTAC CGGTGTGAA ATGTTCC...AA <u>ATGGT</u> TATGCCAGGG <u>GACAACGTAC</u>	119
Agrobacterium tumefaciens	CGACTGTTAC CGGGCGTGAA ATGTTCC...AA <u>ATGGT</u> TATGCC <u>TGGC</u> GACAAC <u>GTCA</u>	147
10 Bacillus subtilis	CAACTGTTAC AGGTGTGAA ATGTTCC...AA <u>ATGGT</u> TATGCC <u>TGGG</u> GATAAC <u>ACTG</u>	148
Bacteroides fragilis	CAGTGTAAAC AGGTGTGAA ATGTTCC...AA <u>ATGGT</u> AA <u>ATGGT</u> GATAAC <u>GTAA</u>	149
15 Borrelia burgdorferi	CTACTGTTAC TGGTGTGAA ATGTTCC...AA <u>ATGGT</u> TATGCC <u>TGGT</u> GATAAT <u>GTTC</u>	150
Brevibacterium linens	CGACTGTCAC CGCTTACGAG ATGTTCC...AG <u>ATGGT</u> CATGCC <u>GGGC</u> GACACC <u>ACCG</u>	151
Burkholderia cepacia	CGACCTGCAAC GGGCGTGAA ATGTTCC...AA <u>ATGGT</u> CATGCC <u>GGGG</u> GACAAC <u>GTGT</u>	152
20 Chlamydia trachomatis	CGATTGTTAC TGGGGTGAA ATGTTCA...AG <u>ATGGT</u> CATGCC <u>TGGG</u> GATAAC <u>GTTG</u>	153
Corynebacterium diphtheriae	CCACCGTTAC CGGTATCGAG ATGTTCC...AG <u>ATGGT</u> CATGCC <u>TGGC</u> GACAAC <u>GTCC</u>	126

127	<i>Corynebacterium genitalium</i>	CCACCGTAC CTCATCGAG ATGTTCA . . AGATGGT TATGCCGGCC GACAACGGTC
128	<i>Corynebacterium jeikeium</i>	CCACCGTAC CTCATCGAG ATGTTCA . . AGATGGT TATGCCGGCC GACAACGGTC
132	<i>Enterococcus faecalis</i>	CAACYGTAC AGGTGTGAA ATGTTCC . . AAATGGT ATGGCTTGT GATAACGGT GACAACGGT . .
5	<i>Enterococcus faecium</i>	CAACAGTAC TGGGTGAA ATGTTCC . . AAATGGT CATGCCGGT GACAACGGT . .
10	<i>Escherichia coli</i>	CTACCTGTAC TGGGTGAA ATGTTCC . . AGATGGT ATGGCCGGCC GACAACATCA
10	<i>Fibrobacter succinogenes</i>	ACGTCACTAC CGGTGTGAA ATGTTCC . . AAATGGT TACTCCGGT GACACGGTCA
15	<i>Flavobacterium ferrugineum</i>	CTACCGTAC AGGTGTGAG ATGTTCC . . AAATGGT TATGCCCTGGT GATAACACCA
15	<i>Gardnerella vaginalis</i>	CCACCGTAC CTCATCGAG ACCTTCC . . AAATGGT TCGCCAGGC GATCACCGCAA
15	<i>Haemophilus influenzae</i>	CTACTGTAAC GGGGTGAA ATGTTCC . . AAATGGT ATGCCAGGC GATAACATCA
20	<i>Helicobacter pylori</i>	CGACTGTAAAC CGGTGTAGAA ATGTTA . . AAATGGT TATGCCCTGGC GATAATGTGA
20	<i>Listeria monocytogenes</i>	TAGTAGTAAC TGGAGTAGAA ATGTTCC . . AAATGGT AAYGGCTTGT GATAACATTC
25	<i>Micrococcus luteus</i>	CCACTGTAC CGGCATCGAG ATGTTCC . . AGATGGT CATGCCGGC GACAACACCG
159	<i>Mycobacterium tuberculosis</i>	CCACCGTAC CGGTGTGAG ATGTTCC . . AGATGGT CATGCCGGT GACAACACCA
160		

Mycoplasma	CACTTGTAC TGGAA <u>TGAA</u> ATGTICA . . AAATGGT TCTACCTGGT GATAATGCTT	161
genitalium		
Neisseria	CCACCTGTAC CGGGGTGAA ATGTICC . . AAATGGT AATGCCGGT GAGAACGTA	162
gonorrhoeae		
5 Rickettsia	CGACTTGTAC <u>ACGTG</u> AGAA ATGTICA . . AGATGGT TATGCCCTGGA GATAATGCTA	163
prowazekii		
Salmonella	CTACCTGTAC TGGGTGAA ATGTICC . . AGATGGT AATGCCGGC GACAACATCA	164
typhimurium		
Shewanella	CAACGTGTAC TGGTGTAGAA ATGTICC . . AGATGGT AATGCCAGGC GATAACATCA	165
10 putida	CGGTCA <u>TAC</u> CG GGGGGGGAG ATGTICC . . AGATGGT GATGCCGGG GACAACATCG	166
Stigmatella		
aurantiaca		
Staphylococcus	CAACTGTAC AGGTGTGAA ATGTICC . . AAATGGT AATGCCCTGGT GATAACGTTG	140
aureus		
15 Staphylococcus	CAACTGTAC TGGTGTAGAA ATGTICC . . AAATGGT TATGCCCTGGC GACAACGTTG	141
epidermidis		
Streptococcus	CACTTGTAC TGGTGTGAA ATGTICC . . AAATGGT TATGCCCTGGT GATAACGTTA	144
agalactiae		
Streptococcus	CACTTGTAC TGGTGTGAA ATGTICC . . AAATGGT AATGCCCTGGT GATAACGTTA	145
pneumoniae		
20 Streptococcus	CTGTGTGTAC TGGTGTGAA ATGTICC . . AAATGGT TATGCCCTGGT GATAACGTTGA	167
pyogenes		
Thiobacillus	CCACCTGCAC CGGGGTGAA ATGTICA . . AAATGGT CATGCCGGC GATAATGTGA	168
cuprinus		
25 Treponema	CACTTGTAC TGGCATGTGAG ATGTICA . . ACATGGT GAGGCCGGG GATAAACACCA	169
pallidum		

10	Selected <sup>a</sup>	ACIKKIAAC IGGIGTIGAR ATGTT	ATGGT <u>TATGCCIGGI</u> GATAAYRT
9	Schizo- albicans	GTGT <u>CACTAC</u> CGAAGTCAAG TCTGTG . . AGAA <u>GAT</u> TGAGGAGTCC <u>CCTAAGT</u> TG	
8	<i>Candida</i>	GTGT <u>ACCCAC</u> TGAAGTCAAR TCCGTG . . AGRATT GGAGAAAT CCAA <u>AAAT</u> CG	
7	<i>Wolinella</i> succinogenes	CAACCGTAAC TGGCGTTGAG AIGTTC . . AGATGGT TATGCCIGGI GACAACGTTA	120
6	<i>Ureaplasma</i> urealyticum	CTGT <u>GTGTAC</u> AGGAATGAA AIGTTA . . ATTGGT TATGCCIGGI <u>GATGACGTT</u>	171

Selected universal primer	SEQ ID NO:23  ACIRRIAC TGGGTGIGAR ATGTT	SEQ ID NO: 24 <sup>b</sup>  AYRTT ITCICCGGG ATTACCAT
15	<sup>a</sup> sequences <sup>a</sup> .	

The sequence numbering refers to the *E. coli* *tuf* gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

20 a "I" stands for inosine which is a nucleotide analog that can bind to any of the four nucleotides A, C, G or T. "R" and "Y" designate nucleotide positions which are

- b This sequence is the reverse complement of the above tuf sequence.

Annex II: Strategy for the selection from tuf sequences of the amplification primers specific for the genus *Enterococcus* (continues on pages 53 and 54).

314	348	401	435	SEQ
5 <i>Bacillus</i> <i>subtilis</i>	CGCGACACTG <u>AA</u> AAACCATT <u>C</u> ATGATGCCA GTTGA...CGGG ACA <u>AG</u> TAA <u>G</u> TGGT <u>G</u> ACG <u>A</u> AGTGA <u>A</u> AT	148	ID NO	
<i>Bacteroides</i> <i>fragilis</i>	CGCGA <u>T</u> ACTG ATAAACCTT <u>C</u> TGATGCCG GTAGA...ACTGG TGT <u>T</u> ATCC <u>C</u> AT <u>G</u> TGGT <u>G</u> ATG AAAT <u>C</u> GA <u>A</u> AT	149		
<i>Burkholderia</i> <i>cepacia</i>	CGTGCA <u>G</u> TG <u>A</u> CGGCC <u>T</u> T CCT <u>G</u> ATGCCG GTGGA...CGGG CAT <u>C</u> GT <u>G</u> AA <u>G</u> <u>G</u> T <u>G</u> GA <u>A</u> AG AAAT <u>C</u> GA <u>A</u> AT	152		
<i>Chlamydia</i> <i>trachomatis</i>	AGAGAA <u>T</u> TG ACA <u>AG</u> CCTT <u>C</u> TAA <u>T</u> GCCT ATTGA...CGTGG ATT <u>T</u> TA <u>A</u> <u>G</u> T <u>T</u> CGATA <u>A</u> AGT <u>T</u> CA <u>G</u> TT	153		
<i>Corynebacterium</i> <i>diphtheriae</i>	CGTGAG <u>A</u> CG <u>A</u> CA <u>AG</u> CCATT CCT <u>C</u> ATGCCT ATCGA...CGTGG CTC <u>C</u> CT <u>G</u> AA <u>G</u> <u>G</u> T <u>G</u> AG <u>G</u> AC <u>G</u> T <u>G</u> AG <u>A</u> T	126		
15 <i>Enterococcus</i> <u>avium</u>	CGTGATA <u>T</u> CTG ACA <u>AA</u> ACCATT <u>C</u> ATGATGCCA GT <u>C</u> GA...CGTGG ACA <u>AG</u> T <u>T</u> CGC <u>G</u> T <u>G</u> GT <u>G</u> ACG <u>A</u> AGTGA <u>A</u> AT	131		
<i>Enterococcus</i> <i>faecalis</i>	CGTGATA <u>T</u> CTG ACA <u>AA</u> ACCATT <u>C</u> ATGATGCCA GT <u>C</u> GA...CGTGG TGA <u>AG</u> T <u>T</u> CGC <u>G</u> T <u>G</u> GT <u>G</u> ACG <u>A</u> AGTGA <u>A</u> AT	132		
<i>Enterococcus</i> <i>faecium</i>	CGTGACA <u>A</u> CG <u>A</u> CA <u>AA</u> CCATT <u>C</u> ATGATGCCA GTTGA...CGTGG ACA <u>AG</u> T <u>T</u> CGC <u>G</u> T <u>G</u> GT <u>G</u> ACG <u>A</u> AGTGA <u>A</u> GT	133		
20 <i>Enterococcus</i> <i>gallinarum</i>	CGTGATA <u>T</u> CTG ACA <u>AA</u> ACCATT <u>C</u> ATGATGCCA GT <u>C</u> GA...CGTGG ACA <u>AG</u> T <u>T</u> CGC <u>G</u> T <u>G</u> GT <u>G</u> ATG <u>A</u> AGTGA <u>A</u> AT	134		
<i>Escherichia</i> <i>coli</i>	CGTGCG <u>A</u> TTG ACA <u>AA</u> GCC <u>T</u> T CCT <u>G</u> CTGCCG ATCGA...CGGG TAT <u>C</u> AT <u>C</u> AA <u>G</u> T <u>G</u> GA <u>A</u> AG AAAT <u>C</u> GA <u>A</u> AT	154		

<i>Gardnerella vaginalis</i>	CACGATCTG ACAAGCCATT CTTGATGCCA ATCGA... CGTGG TAAGCTCCCA ATCAACACCC <u>CAGTTGAGAT</u> 135
<i>Haemophilus influenzae</i>	CGTGCATTG ACCAACCGTT CCTTCTTCCA ATCGA... CGAGG TATTATCCGT ACAGGTGATG <u>AAGTGAAT</u> 157
<i>5 Helicobacter pylori</i>	AGAGACACTG <u>AAAAA</u> ACTT CTTGATGCCG GTTGA... AGAGG CGTGGCGATG <u>GTAGGGAA</u> AAGTGGAAAT 158
<i>Listeria monocytogenes</i>	CGTGATACTG ACAAAACCATT CATGATGCCA GTTGA... CGTGG ACAAGTAAA <u>GTGGTGACG</u> AAGTGAAGT 138
<i>10 Micrococcus luteus</i>	CGCGACAAAGG ACAAGGCCGTI CCTGATGCCG ATCGA... CGCGG CACCCCTGAG <u>ATCAACTCCG</u> AGGTGAGAT 159
<i>Mycobacterium tuberculosis</i>	CGCGGAGCCG <u>ACAAGCCGTI</u> CCTGATGCCG GTCGA... CGCGG CGTGATCAAC <u>GTGAACCGAGG</u> AAGTGAAGT 160
<i>Mycoplasma genitalium</i>	CGTGAAGTAG ATAAACCTT CCTTATAGCA ATTGA... AGAGG TGAACTCAA <u>GTAGGTCAAG</u> AAGTGAAT 161
<i>15 Neisseria gonorrhoeae</i>	CGTGCCTGG <u>ACAAACCA</u> CCTGCTGCCT ATCGA... CGAGG TATCATCCAC <u>GTGGGTGACG</u> AGAT <del>T</del> GAAT 162
<i>Salmonella typhimurium</i>	CGTGCCTGG <u>ACAAACCA</u> CCTGCTGCCA ATCGA... CGCGG TATCATCAA <u>GTGGGGAA</u> AAGTGAAT 164
<i>Shewanella putida</i>	CGTGACATCG ATAAGCCGTI CCTACTGCCA ATCGA... CGTGG TATTGTACGC <u>GTAGGGGACG</u> AAGTGAAT 165
<i>20 Staphylococcus aureus</i>	CGTGAATCTG ACAAAACCATT CATGATGCCA GTTGA... CGTGG TCAAATCAA <u>GTGGGTGAG</u> AAGTGAAT 140
<i>Staphylococcus epidermidis</i>	CGTGATCTG ACAAAACCATT CATGATGCCA GTTGA... CGTGG TCAAATCAA <u>GTGGGTGAG</u> AAGTGAAT 141
<i>25 Staphylococcus saprophyticus</i>	CGTGAATCTG ACAAAACCATT CATGATGCCA GTTGA... CGTGG TCAAATCAA <u>GTGGGGAA</u> AATCGARAT 142

*Streptococcus agalactiae* CGTGACTTG ACAAAACCTT ACTTCTTCCA GTTGA... CGTGG TACTGTTCGT GTCAACGACG AAGTTGAAT 144  
*Streptococcus pneumoniae* CGTGACACTG ACAAAACCATT GCTTCTTCCA GTCGA... CGTGG TATC~~GT~~AAA GTCAACGACG AAATCGAAAT 145  
 5 *Streptococcus pyogenes* CGCGACACTG ACAAAACCATT GCTTCTTCCA GTCGA... CGTGG TACTGTTCGT GTCAACGACG AAATCGAAAT 167  
*Ureaplasma urealyticum* CGTAGTACTG ACAAAACCATT CTTATAGCA ATTGA... CGTGG TGTTTAAA GTTAATGATG AGGTGAAT 170  
 Selected TACTG ACAAAACCATT CATGATG GTTGGC GTTGGCTGACG AAGT<sup>a</sup>  
 10 sequences  
 Selected SEQ ID NO: 13 SEQ ID NO: 14<sup>a</sup>  
 genus-specific primer TACTG ACAAAACCATT CATGATG AACTTC GTCACCAACG CGAAC  
 15 sequences:  
 20 \* This sequence is the reverse complement of the above *tuf* sequence.

The sequence numbering refers to the *E. faecalis* *tuf* gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

NOTE: The above primers also amplify *tuf* sequences from *Abiotrophia* species; this genus has recently been related to the *Enterococcus* genus by 16S rRNA analysis.

Annex III: Strategy for the selection from tuf sequences of the amplification primers specific for the genus *Staphylococcus* (continues on pages 56 and 57).

		385	420 . . . 579	611 SEQ ID
5	Bacillus subtilis	TGCCC <u>G</u> TGA <u>GA</u> ACGGGAC <u>AA</u> GTT <u>AA</u> ACT CGG . . . TTG CTA <u>AA</u> CC <u>AG</u> G <u>T</u> ACAT <u>CA</u> T <u>CC</u> ACAC <u>AG</u> CA 148		NO
	Bacteroides fragilis	AGGT <u>CG</u> TATC <u>GA</u> AA <u>CT</u> GG <u>GT</u> <u>T</u> AT <u>CC</u> AT <u>GT</u> AGG . . . TTT GTAA <u>CC</u> GG <u>T</u> CA <u>G</u> ATT <u>AA</u> <u>C</u> CT <u>CA</u> CT <u>CT</u> TA 149		
	Burkholderia cepacia	GGGT <u>CG</u> TG <u>TC</u> <u>G</u> AG <u>CG</u> GG <u>CA</u> <u>T</u> GT <u>GA</u> GG <u>T</u> CGG . . . TGG CGA <u>AG</u> GG <u>GG</u> <u>T</u> CC <u>AT</u> C <u>AG</u> <u>CC</u> GG <u>AC</u> AC <u>GG</u> 152		
10	Chlamydia trachomatis	TG <u>AC</u> GT <u>AT</u> <u>G</u> AC <u>CG</u> T <u>GG</u> <u>AA</u> <u>T</u> GT <u>TT</u> <u>AA</u> ACT TTC . . . TTT GCT <u>TC</u> CC <u>AA</u> <u>C</u> AG <u>TC</u> TT <u>AA</u> <u>C</u> CT <u>CA</u> AC <u>AC</u> 153		
	Corynebacterium diphtheriae	CGGCC <u>CG</u> T <u>GT</u> <u>T</u> AC <u>CG</u> GG <u>GT</u> <u>C</u> CT <u>GA</u> GG <u>GT</u> CAA . . . TTG TTA <u>AG</u> CC <u>AG</u> G <u>C</u> CT <u>TA</u> C <u>AC</u> C <u>CC</u> G 126		
15	Enterococcus faecalis	AGGA <u>CG</u> T <u>GT</u> <u>T</u> AA <u>CG</u> GG <u>GT</u> <u>A</u> GT <u>TC</u> GG <u>GT</u> TGG . . . TAG CTA <u>AA</u> CC <u>AG</u> G <u>T</u> AC <u>AT</u> C <u>AC</u> T <u>CC</u> ACAC <u>CA</u> 132		
	Enterococcus faecium	AGGT <u>CG</u> T <u>GT</u> <u>T</u> AA <u>CG</u> GG <u>AC</u> <u>A</u> GT <u>TC</u> GG <u>GT</u> TGG . . . TAG CTA <u>AA</u> CC <u>AG</u> G <u>T</u> AC <u>AT</u> C <u>AC</u> A <u>C</u> CT <u>GT</u> TA <u>CA</u> A 133		
	Escherichia coli	CGGT <u>CG</u> T <u>GT</u> <u>T</u> AA <u>CG</u> GG <u>GT</u> <u>T</u> CA <u>T</u> AA <u>AG</u> T TGG . . . TGG CTA <u>AG</u> GG <u>GG</u> <u>T</u> AC <u>AT</u> C <u>AC</u> A <u>CC</u> GG <u>AC</u> AC <u>CC</u> A 154		
20	Gardnerella vaginalis	CGGT <u>CG</u> T <u>GT</u> <u>T</u> AC <u>CG</u> GG <u>GT</u> <u>A</u> G <u>CT</u> CC <u>AA</u> T CAA . . . TGG CT <u>GT</u> TC <u>CC</u> GG <u>T</u> CT <u>GT</u> GA <u>T</u> CC <u>AC</u> AC <u>CC</u> A 135		

<i>Haemophilus influenzae</i>	AGCTCGTGT <u>GAACGAGGTA</u> <u>TTATCCGTAC</u> AGG. . . . TAG CGAAC <u>CCAGG</u> <u>TTCAATCACA</u> <u>CCACACACTG</u> 157
<i>Helicobacter pylori</i>	AGGTAGGAT <u>AAAAAGGGCG</u> <u>TGGTGAAGT</u> AGG. . . . TAT GCAAA <u>CCAGG</u> <u>TTCTATCACT</u> <u>CGGCACAAAGA</u> 158
<i>5 Listeria monocytogenes</i>	TGGACGTGT <u>GAACGIGGAC</u> <u>AACTAAAGT</u> TGG. . . . TAG CTA <u>AAACCGG</u> <u>TTCGATTACT</u> <u>CCACACACTA</u> 138
<i>Micrococcus luteus</i>	CGGT <u>CGGCC</u> <u>GAGCGGGCA</u> <u>CCCTGAAGAT</u> CAA. . . . TGG TGG <u>AGCCGG</u> <u>CTCCATCACC</u> <u>CGGCACACCA</u> 159
<i>10 Mycobacterium tuberculosis</i>	CGGAC <u>GTG</u> <u>GACCGGGCG</u> <u>TGATCAACGGT</u> GAA. . . . TCA CCA <u>AGCCGG</u> <u>CACCAACCGG</u> <u>CCGCACACCG</u> 160
<i>Mycoplasma genitalium</i>	AGGA <u>AGAGT</u> <u>GAAGAGGTG</u> <u>AACTCAAAAGT</u> AGG. . . . TAG CAA <u>AAACCGG</u> <u>CTCTTAA</u> <u>CGGCACAAAGA</u> 161
<i>Neisseria gonorrhoeae</i>	CGGCC <u>GTGT</u> <u>GAGCGGGTA</u> <u>TCATCCACGT</u> TGG. . . . TGG CAA <u>ACGGGG</u> <u>TACTATCACT</u> <u>CTCACACCCA</u> 162
<i>15 Salmonella typhimurium</i>	CGGT <u>CGTGT</u> <u>GAGCGGGTA</u> <u>TGTTACGCGT</u> AGG. . . . TAG CGA <u>AGCCGG</u> <u>TCACATCAAC</u> <u>CCGCACACCA</u> 164
<i>Shewanella putida</i>	AGGT <u>CGTGT</u> <u>GAACGIGGTC</u> <u>AAATCAAAAGT</u> TGG. . . . TAG CTG <u>CTCCCTGG</u> <u>TTCAATTACA</u> <u>CCACACACTA</u> 165
<i>20 Staphylococcus aureus</i>	AGGCC <u>GTGT</u> <u>GAACGIGGTC</u> <u>AAATCAAAAGT</u> TGG. . . . TAG CTG <u>CTCCCTGG</u> <u>TTCAATTACA</u> <u>CCACACACTG</u> 140
<i>Staphylococcus epidermidis</i>	AGGCC <u>GTGT</u> <u>GAACGIGGTC</u> <u>AAATCAAAAGT</u> CGG. . . . TAG CTG <u>CTCCCTGG</u> <u>TACTATCACA</u> <u>CCACACACAA</u> 141
<i>25 Staphylococcus saprophyticus simulans</i>	AGGCC <u>GTGT</u> <u>GAACGIGGTC</u> <u>AAATCAAAAGT</u> CGG. . . . TAG CAG <u>CTCCCTGG</u> <u>CTCTTAA</u> <u>CCACACACAA</u> 143

<i>Streptococcus agalactiae</i>	AGGACGTATC <u>GACCGTGT</u> CTC <u>GTG</u> GTGT CAA. . . TTG C <u>TAACC</u> GG <u>TTC</u> AA <u>TC</u> AA <u>AC</u> CCACACACTA	144
<i>Streptococcus pneumoniae</i>	AGGACGTATC <u>GACCGTGT</u> T <u>CGT</u> TA <u>AA</u> CT CAA. . . TCG C <u>TAACC</u> GG <u>TTC</u> AA <u>TC</u> AA <u>AC</u> CCACACACTA	145
<i>Ureaplasma urealyticum</i>	TGGACGTGT <u>GAACGTGT</u> T <u>AT</u> TA <u>AA</u> GT TAA. . . TTG T <u>AAAC</u> GG <u>ATC</u> AA <u>TTAA</u> <u>C</u> T <u>CA</u> <u>CC</u> GT <u>A</u>	170
Selected sequences <sup>a</sup>	CCGTGT <u>GAACGTGT</u> AA <u>AT</u> CAA	
Selected sequences <sup>a</sup>	GCTCCTGG <u>Y</u> WCWATYACA CCACAYA	

10 Selected sequences <sup>a</sup>	SEQ ID NO: 17
genus-specific primer	CCGTGT <u>GAACGTGT</u> AA <u>AT</u> CAA
Selected sequences <sup>a</sup>	SEQ ID NO: 18 <sup>b</sup>
genus-specific primer	TRTGTGT <u>GTRATGWRC</u> CAGGAGC

15 The sequence numbering refers to the *S. aureus* *tuf* gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

<sup>a</sup> "R", "W" and "Y" designate nucleotide positions which are degenerated. "R" stands for A or G; "W", for A or T; "Y", for C or T.

<sup>b</sup> This sequence is the reverse complement of the above *tuf* sequence.

Annex IV: Strategy for the selection from tuf sequences of the amplification primers specific for the species *Candida albicans* (continues on pages 59 and 60).

		58	90	181	213	SEQ ID NO
<i>Candida</i>	<i>albicans</i>	CGTCAAGAAG <u>GTGGT</u> TACA ACCCAAAGAC TGT...CAA <u>ATCCGGT</u> AA <u>GT</u> TACTGGTA <u>AGAC</u> CTTGT				120
<i>Candida</i>		CAT <u>CAAGAAG</u> <u>GTGGT</u> TACA ACCCAAAGAC TGT...CAA <u>GGCTGGT</u> GTC <u>GTCA</u> AGGGTA AGAY <u>CT</u> TGT				121
5	<i>glabrata</i>	CAT <u>CAAGAAG</u> <u>GTGGT</u> TACA ACCCAAAGAC TGT...CAA <u>GGCA</u> GGTGT <u>GT</u> TAAGGGTA AGACCTTATT				122
<i>Candida</i>						
<i>krusei</i>						
<i>Candida</i>		CGTCAAGAAG <u>GTGGT</u> TACA ACC <u>CTAA</u> GGC TGT...TAA <u>AGCTGGT</u> AAG <u>GT</u> TACCGGT <u>AGAC</u> CTTGT				123
<i>parapsilosis</i>						
10	<i>Candida</i>	CGT <u>CAAGAAG</u> <u>GTGGT</u> TACA ACC <u>CTAA</u> GGC TGT...CAA <u>GGCTGGT</u> AAG <u>GT</u> TACCGGT <u>AGAC</u> CTTGT				124
<i>tropicalis</i>						
<i>Schizo-</i>						
<i>saccharomyces pombe</i>						
<i>Human</i>		GGAGATCCGG <u>GAGCTGCT</u> CA CGCAGTTGG CTA...GTT AGG <u>CTG</u> CAAG TCT <u>GTG</u> CGAG AGCTACTGG				
15	<i>Chlamydia</i>	GGAGCTGCC <u>GAGCTGCT</u> CA GCAAGT <u>ACGG</u> CTT...CAA ATG.....TAT <u>TC</u> GG AGCTGTATGAA				153
<i>trachomatis</i>						
<i>Corynebacterium</i>		GGAGATCCRT <u>GAGCTGCT</u> CG CTGAGCCAG TTA...GAA GTGGACCCAG TCCATCATCG ACCT <u>CT</u> ATGCA				126
<i>diphtheriae</i>						
<i>Enterococcus</i>		GGAA <u>GTT</u> CGT <u>GACTT</u> AT CAGA <u>ATA</u> CGA TTT.....TGAA <u>GA</u> AAA <u>ATCT</u> AG AATTA <u>AT</u> GGC				132
20	<i>faecalis</i>					
<i>Escherichia</i>	<i>coli</i>	GGAA <u>GTT</u> CGT <u>GACTT</u> GT CT <u>CA</u> GTACGA CTT.....GG <u>GA</u> GGC <u>AA</u> AT <u>CC</u> TGG AACTGGTGG				154

Flavobacterium	CGAGGTTCGC <u>GAAGAACTGA</u> CTA <u>AA</u> CGCGG TTT . . . . .	GG <u>CTTAAA</u> <u>GAATTTGAAA</u> ACCTGATGGA	156
<i>ferrugineum</i>			
<i>Gardnerella</i>	AGAGGTCGGT <u>GACCTCCCTCG</u> <u>AAGAAAACGG</u> CTT . . . CAA	<u>GTGGTAGAG</u> ACCGTCAAGG <u>AACTCATGAA</u>	135
<i>vaginalis</i>			
5 <i>Haemophilus</i>	GGAGGTTCGT <u>GAACCTCTAT</u> C <u>TCA</u> ATATGA CTT . . . . .	GG <u>AAAGAA</u> <u>AAAATCCTTG</u> AGTTAGAAA	157
<i>influenzae</i>			
<i>Listeria</i>	GGAA <u>ATT</u> CGT <u>GATCTTAA</u> CT <u>GA</u> ATATGA ATT . . . . .	GG <u>GAAGCT</u> AAA <u>ATTGACG</u> <u>AGTTAATGGA</u>	138
<i>monocytogenes</i>			
Micrococcus	GGAA <u>GT</u> CCGT <u>GAGTTGCTGG</u> C <u>TG</u> CC <u>AGGA</u> ATT . . . CAA	<u>GTGGGTGAG</u> T <u>C</u> <u>TG</u> TCAAC <u>C</u> <u>AGTTGATGGA</u>	159
10 <i>luteus</i>	GGAA <u>AT</u> CCGC <u>GACCTGGCTGT</u> C <u>CA</u> GCTACGA CTT . . . . .	GG <u>AAAGAA</u> <u>AAAATCTCG</u> <u>AACTGGCTAC</u>	162
<i>Neisseria</i>			
<i>gonorrhoeae</i>	GGAA <u>GT</u> TCG <u>GAAC</u> GGCTGT C <u>TG</u> AGTACGA CTT . . . . .	GG <u>GAAGCG</u> AAA <u>ATCATCG</u> <u>AACTGGCTGG</u>	164
<i>Salmonella</i>			
<i>typhimurium</i>	GGAGGTTCGT <u>GACTTAA</u> G <u>GG</u> AA <u>ATGAA</u> CTT . . . . .	GG <u>GAAGAA</u> <u>AAAATCTAG</u> <u>AAATAATGGA</u>	140
15 <i>Staphylococcus</i>	GGAA <u>AT</u> CCGT <u>GACCTATGT</u> C <u>AGG</u> AA <u>ATCGA</u> CTT . . . . .	GG <u>AAAGAC</u> <u>ATCGTTATGG</u> <u>AAATTGATGAA</u>	145
<i>aureus</i>			
<i>Streptococcus</i>			
<i>pneumoniae</i>	AGAGGTTGGT <u>GATGGCTTG</u> C <u>TG</u> GA <u>ATATGG</u> GTT . . . GGA	<u>GGATGGAGCT</u> <u>TGATTTGAGG</u> <u>AACTGCTTGC</u>	169
20 <i>Treponema</i>			
<i>pallidum</i>			

Selected sequences  
CAAGAAG GTGGGTACA ACCCAAAGA  
ATCCGGTAAA GTTACTGGTA AGACCT

Selected 5 species-specific primer sequences:  
SEQ ID NO: 11 SEQ ID NO: 12<sup>a</sup>  
CAAGAAG GTGGGTACA ACCCAAAGA  
AGGTCTTACC AGTAACTTAC CGGAT

10 The sequence numbering refers to the *Candida albicans* tuf gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

<sup>a</sup> This sequence is the reverse-complement of the above tuf sequence.

Annex V: Strategy for the selection from the *recA* gene of the amplification primers specific for the genus *Streptococcus* (continues on pages 62 and 63).

		574 SEQ	ID NO
415	449...540		
5. <i>Bordetella pertussis</i>	CTCGAGATCA <u>CCGACGGCT</u> <u>GGCGGCTCG</u> GGCTC...GGCCC GC <u>CTGATGAG</u> CC <u>AGGCCGCTG</u> CG <u>CAAGGCTGA</u>		
<i>Burkholderia cepacia</i>	CTCGAAATCA <u>CCGATGGCT</u> <u>GGCGGCTCG</u> GGCTC...GGCCC GC <u>CTGATGTC</u> GC <u>AGGGGCTG</u> CG <u>CAAGGCTGA</u>		
10 <i>Campylobacter jejuni</i>	TTAGAAATTG <u>TAGAAACTAT</u> AGCAAGAA <u>GT</u> GGGC...AGCAA GACT <u>TA</u> GTC TCA <u>AGCTCTA</u> AG <u>AA</u> ACTTA		
<i>Chlamydia trachomatis</i>	TT <u>CAGTATTG</u> <u>CAGAGCTCTT</u> AG <u>GGCGTTCT</u> GG <u>AGC</u> ...AGCTC GC <u>ATGATGTC</u> GC <u>AGGCTCTA</u> CG <u>CAATTAA</u>		
<i>Clostridium perfringens</i>	TTAGAAATAA <u>CAGAAGCTT</u> AG <u>TTAGATCA</u> GG <u>AGC</u> ...AGCTA GATT <u>ATGTC</u> ACA <u>AGCTTA</u> AG <u>AAAGTTAA</u>		
15 <i>Corynebacterium pseudotuberculosis</i>	CTGGAGAT <u>G</u> <u>AGATATGCT</u> TG <u>TCGCTCT</u> GG <u>AGC</u> ...AG <u>GGC</u> GT <u>TGATGAG</u> TC <u>AGGCCGCTG</u> CG <u>TAAGGATGA</u>		
<i>Enterobacter agglomerans</i>	CTCGAAATCT <u>GTGATGGCT</u> <u>GACCGTTCA</u> GG <u>GC</u> ...AGCTC GT <u>ATGATGAG</u> CC <u>AGGCCGATG</u> CG <u>TAAGGCTTG</u>		
<i>Enterococcus faecium</i>	TT <u>AGAGATTG</u> <u>CCGATGCC</u> AG <u>TTCAAGT</u> GGT <u>GC</u> ...AGCTC GACT <u>ATGTC</u> TCA <u>AGCCACTA</u> CG <u>TAATTAT</u>		
20 <i>Escherichia coli</i>	CTGGAAATCT <u>GTGACGCC</u> <u>GGCGGTTCT</u> GG <u>GC</u> ...GG <u>CAC</u> GT <u>ATGATGAG</u> CC <u>AGGCCGATG</u> CG <u>TAAGGCTGG</u>		

Haemophilus influenzae	GGCAACAGAA GAATAGAATT TAAATGCAATT ACCGC... GACCT GTGAGTTAC <u>GC</u> AAAGGT <u>TG</u> AGACATTAA
<i>Helicobacter pylori</i>	TTAGAAATT TAGAAACGAT CACCGAAGC GGNGG... AGCAA GCCTATGAG CCATGGTTA AGAAAATTCA
<i>S Lactococcus lactis</i>	CTTCAAATG CTGAAAATT GATTACTCT <u>GG</u> TGCGTCT GCAGC... AGCAC GTATGAT <u>TG</u> ACAAGCCATG CGTAAACTTG
<i>Legionella pneumophila</i>	CTGGAAATT CTGATATGCT <u>GG</u> TGCGTCT GCAGC... GGCAA GATTGAT <u>TG</u> CCAAGCC <u>TG</u> CGTAAATTGA
<i>Mycoplasma genitalium</i>	TTTGCTCTTA TCGATATCATT AATTAAAACA AACAA... TGCAA GAATGAT <u>TG</u> AAAAGGT <u>TG</u> CGAAGAAATAC
<i>Neisseria gonorrhoeae</i>	TTGGAAATCT GCGCACCGCT <u>CG</u> TCCGRTCG GGGG... GGGC GCCTGATGAG TCAGGCT <u>TG</u> CGGAAACTGA
<i>Proteus mirabilis</i>	CTGAAATT GTGATGCCATT ATCTCGCTCT GGTGC... CGCAC GTATGATGAG CCAAGGT <u>TG</u> CGTAAACTAG
<i>Pseudomonas aeruginosa</i>	CTGGAAATCA CCGACATGCT <u>GG</u> TGCGCTCC AACGC... GGCAC GCCTGAT <u>TG</u> CCAGGGCG <u>TG</u> CGGAAAGATCA
<i>Serratia marcescens</i>	CTGGAAATCT GTGATGCCGT GACCCGCTCC GGGC... GGGC GCATGATGAG CCAGGGCATG CGTAAAGCTGG
<i>Shigella flexneri</i>	CTGGAAATCT GTGAGCCCT <u>GG</u> CCGCGTCT GGGC... GGCAC GTATGATGAG CCAGGGATG CGTAAAGCTGG
<i>Staphylococcus aureus</i>	CTTGAATCG CCGAACATT TGTAGAAGT GGTGC... AGCTC GTTAAATG <u>TG</u> ACAAGCGTTA CGTAAACTTT
<i>Streptococcus gordonii</i>	TTAGAAATG CAGGAAATT GATTGACTCT GGGC.....
<i>S Streptococcus mitrans</i>	CTTGAATCG CAGGAAATT GATTGATCT GGGC... AGCAC GCATGATGAG TCAAGGGATG CGTAAATTAT

<i>Streptococcus pneumoniae</i>	CTTGAGATG <u>CGGGAAATT</u> GATTGACTCA GGTGC...GGCTC <u>GTATGATGAG</u> CCAGGCCATG <u>CGTAAACRTG</u> 34
<i>Streptococcus pyogenes</i>	CTTGAATTG <u>CAGGTAATT</u> GATTGATTCT GGTGC...AGCAC <u>GTATGATGAG</u> TCAGGCCATG <u>CGTAAATTAT</u> 35
5 <i>Streptococcus salivarius</i>	CTCGAAATTG <u>CAGGTAAGCT</u> GATTGACTCT GGTGC...AGGCC <u>GTATGATGAG</u> TCAAGCCATG <u>CGTAAACRTT</u> 36
<i>Vibrio cholerae</i>	CTGGAAATT <u>GTGATGCACT</u> GGGTCGCTCT GGTGC...AGCGC <u>GTATGTTGTC</u> GCAAGCAATG <u>CGTAAACTGA</u>
<i>Yersinia pestis</i>	CTGGAAATT <u>GTGATGGCT</u> <u>GACTCGCTCT</u> GGTGC...CGCGC <u>GTATGATGAG</u> CCAGGCCATG <u>CGTAAAGCTGG</u>
10 Selected sequences <sup>a</sup>	<u>GAAATTG</u> <u>CAGGIAATT</u> <u>GATTGA</u> ATGATGAG TCAIGGCCATG <u>CGTAA</u>
Selected sequences <sup>a</sup>	SEQ ID NO: 21 SEQ ID NO: 22 <sup>b</sup>
15 genus-specific primer sequences <sup>a</sup> :	GAAATTG CAGGIAATT GATTGA TTACGGCAT GGCITGACTC ATCAT

The sequence numbering refers to the *S.pneumoniae* *recA* sequence. Underlined nucleotides are identical to the selected sequence or match that sequence.

- <sup>a</sup> "I" stands for inosine which is a nucleotide analog that can bind to any of the four nucleotides A, C, G or T.
- <sup>b</sup> This sequence is the reverse complement of the above *recA* sequence.

## Annex VI: Specific and ubiquitous primers for DNA amplification

	SEQ ID NO	Nucleotide sequence	Originating DNA fragment	
			SEQ ID NO	Nucleotide position
<u>Bacterial species: Enterococcus faecium</u>				
5	1	5'-TGC TTT AGC AAC AGC CTA TCA G	26 <sup>a</sup>	273-294
	2 <sup>b</sup>	5'-TAA ACT TCT TCC GGC ACT TCG	26 <sup>a</sup>	468-488
<u>Bacterial species: Listeria monocytogenes</u>				
10	3	5'-TGC GGC TAT AAA TGA AGA GGC	27 <sup>a</sup>	339-359
	4 <sup>b</sup>	5'-ATC CGA TGA TGC TAT GGC TTT	27 <sup>a</sup>	448-468
<u>Bacterial species: Neisseria meningitidis</u>				
15	5	5'-CCA GCG GTA TTG TTT GGT GGT	28 <sup>a</sup>	56-76
	6 <sup>b</sup>	5'-CAG GCG GCC TTT AAT AAT TTC	28 <sup>a</sup>	212-232
<u>Bacterial species: Staphylococcus saprophyticus</u>				
20	7	5'- AGA TCG AAT TCC ACA TGA AGG TTA TTA TGA	29 <sup>c</sup>	290-319
	8 <sup>b</sup>	5'- TCG CTT CTC CCT CAA CAA TCA AAC TAT CCT	29 <sup>c</sup>	409-438
<u>Bacterial species: Streptococcus agalactiae</u>				
25	9	5'-TTT CAC CAG CTG TAT TAG AAG TA	30 <sup>a</sup>	59-81
	10 <sup>b</sup>	5'-GTT CCC TGA ACA TTA TCT TTG AT	30 <sup>a</sup>	190-212
<u>Fungal species: Candida albicans</u>				
30	11	5'-CAA GAA GGT TGG TTA CAA CCC AAA GA	120 <sup>c</sup>	61-86
	12 <sup>b</sup>	5'-AGG TCT TAC CAG TAA CTT TAC CGG AT	120 <sup>c</sup>	184-209

<sup>a</sup> Sequences from databases.<sup>b</sup> These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.<sup>c</sup> Sequences determined by our group.

Annex VI: Specific and ubiquitous primers for DNA amplification  
(continues on next page)

SEQ ID NO	Nucleotide sequence	Originating DNA fragment	
		SEQ ID NO	Nucleotide position
5	<u>Bacterial genus: Enterococcus</u>		
13	5'-TAC TGA CAA ACC ATT CAT GAT G	131-134 <sup>a,b</sup>	319-340 <sup>c</sup>
14 <sup>d</sup>	5'-AAC TTC GTC ACC AAC GCG AAC	131-134 <sup>a,b</sup>	410-430 <sup>c</sup>
10	<u>Bacterial genus: Neisseria</u>		
15	5'-CTG GCG CGG TAT GGT CGG TT	31 <sup>e</sup>	21-40 <sup>f</sup>
16 <sup>d</sup>	5'-GCC GAC GTT GGA AGT GGT AAA G	31 <sup>e</sup>	102-123 <sup>f</sup>
15	<u>Bacterial genus: Staphylococcus</u>		
17	5'-CCG TGT TGA ACG TGG TCA AAT CAA A	140-143 <sup>a,b</sup>	391-415 <sup>g</sup>
18 <sup>d</sup>	5'-TRT GTG GTG TRA TWG WRC CAG GAG C	140-143 <sup>a,b</sup>	584-608 <sup>g</sup>
19	5'-ACA ACG TGG WCA AGT WTT AGC WGC T	140-143 <sup>a,b</sup>	562-583 <sup>g</sup>
20	5'-ACC ATT TCW GTA CCT TCT GGT AAG T	140-143 <sup>a,b</sup>	729-753 <sup>g</sup>
20	<u>Bacterial genus: Streptococcus</u>		
21	5'-GAA ATT GCA GGI AAA TTG ATT GA	32-36 <sup>e</sup>	418-440 <sup>h</sup>
22 <sup>d</sup>	5'-TTA CGC ATG GCI TGA CTC ATC AT	32-36 <sup>e</sup>	547-569 <sup>h</sup>
25	<u>Universal primers</u>		
23	5'-ACI KKI ACI GGI GTI GAR ARG TT	118-146 <sup>a,b</sup> 147-171 <sup>a,e</sup>	493-515 <sup>i</sup>
24 <sup>d</sup>	5'-AYR TTI TCI CCI GGC ATI ACC AT	118-146 <sup>a,b</sup> 147-171 <sup>a,e</sup>	778-800 <sup>i</sup>

30 <sup>a</sup> These sequences were aligned to derive the corresponding primer.

<sup>b</sup> *tuf* sequences determined by our group.

<sup>c</sup> The nucleotide positions refer to the *E. faecalis* *tuf* gene fragment (SEQ ID NO: 132).

35 <sup>d</sup> These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

<sup>e</sup> Sequences from databases.

<sup>f</sup> The nucleotide positions refer to the *N. meningitidis* *asd* gene fragment (SEQ ID NO: 31).

<sup>g</sup> The nucleotide positions refer to the *S. aureus* tuf gene fragment (SEQ ID NO: 140).

<sup>h</sup> The nucleotide positions refer to the *S. pneumoniae* recA gene (SEQ ID NO: 34).

5      <sup>i</sup> The nucleotide positions refer to the *E. coli* tuf gene fragment (SEQ ID NO: 154).

## Annex VI: Specific and ubiquitous primers for DNA amplification

	SEQ ID NO	Nucleotide sequence	Originating DNA fragment	
			SEQ ID	Nucleotide
			NO	position
<u>Antibiotic resistance gene: bla<sub>tem</sub></u>				
5	37	5'-CTA TGT GGC GCG GTA TTA TC	-	-
	38	5'-CGC AGT GTT ATC ACT CAT GG	-	-
	39	5'-CTG AAT GAA GCC ATA CCA AA	-	-
10	40	5'-ATC AGC AAT AAA CCA GCC AG	-	-
<u>Antibiotic resistance gene: bla<sub>shv</sub></u>				
	41	5'-TTA CCA TGA GCG ATA ACA GC	-	-
15	42	5'-CTC ATT CAG TTC CGT TTC CC	-	-
	43	5'-CAG CTG CTG CAG TGG ATG GT	-	-
	44	5'-CGC TCT GCT TTG TTA TTC GG	-	-
<u>Antibiotic resistance gene: bla<sub>rob</sub></u>				
20	45	5'-TAC GCC AAC ATC GTG GAA AG	-	-
	46	5'-TTG AAT TTG GCT TCT TCG GT	-	-
	47	5'-GGG ATA CAG AAA CGG GAC AT	-	-
25	48	5'-TAA ATC TTT TTC AGG CAG CG	-	-
<u>Antibiotic resistance gene: bla<sub>oxa</sub></u>				
	49	5'-GAT GGT TTG AAG GGT TTA TTA TAA G	110 <sup>a</sup>	686-710
30	50 <sup>b</sup>	5'-AAT TTA GTG TGT TTA GAA TGG TGA T	110 <sup>a</sup>	802-826
<u>Antibiotic resistance gene: bla<sub>Z</sub></u>				
	51	5'-ACT TCA ACA CCT GCT GCT TTC	111 <sup>a</sup>	511-531
35	52 <sup>b</sup>	5'-TGA CCA CTT TTA TCA GCA ACC	111 <sup>a</sup>	663-683
<u>Antibiotic resistance gene: aadB</u>				
	53	5'-GGC AAT AGT TGA AAT GCT CG	-	-
40	54	5'-CAG CTG TTA CAA CGG ACT GG	-	-
<u>Antibiotic resistance gene: aacC1</u>				
	55	5'-TCT ATG ATC TCG CAG TCT CC	-	-
45	56	5'-ATC GTC ACC GTA ATC TGC TT	-	-

<sup>a</sup> Sequences from databases.<sup>b</sup> These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

## Annex VI: Specific and ubiquitous primers for DNA amplification

	SEQ ID NO	Nucleotide sequence	Originating DNA fragment	
			SEQ ID	Nucleotide
			NO	position
<u>Antibiotic resistance gene: aacC2</u>				
5	57	5'-CAT TCT CGA TTG CTT TGC TA	-	-
	58	5'-CCG AAA TGC TTC TCA AGA TA	-	-
<u>Antibiotic resistance gene: aacC3</u>				
10	59	5'-CTG GAT TAT GGC TAC GGA GT	-	-
	60	5'-AGC AGT GTG ATG GTA TCC AG	-	-
<u>Antibiotic resistance gene: aac6'-IIa</u>				
15	61	5'-GAC TCT TGA TGA AGT GCT GG	112 <sup>a</sup>	123-142
	62 <sup>b</sup>	5'-CTG GTC TAT TCC TCG CAC TC	112 <sup>a</sup>	284-303
20	63	5'-TAT GAG AAG GCA GGA TTC GT	112 <sup>a</sup>	445-464
	64 <sup>b</sup>	5'-GCT TTC TCT CGA AGG CTT GT	112 <sup>a</sup>	522-541
<u>Antibiotic resistance gene: aacA4</u>				
25	65	5'-GAG TTG CTG TTC AAT GAT CC	-	-
	66	5'-GTG TTT GAA CCA TGT ACA CG	-	-
<u>Antibiotic resistance gene: aad(6')</u>				
30	173	5'-TCT TTA GCA GAA CAG GAT GAA	-	-
	174	5'-GAA TAA TTC ATA TCC TCC G	-	-
<u>Antibiotic resistance gene: vanA</u>				
35	67	5'-TGT AGA GGT CTA GCC CGT GT	-	-
	68	5'-ACG GGG ATA ACG ACT GTA TG	-	-
	69	5'-ATA AAG ATG ATA GGC CGG TG	-	-
	70	5'-TGC TGT CAT ATT GTC TTG CC	-	-
<u>Antibiotic resistance gene: vanB</u>				
40	71	5'-ATT ATC TTC GGC GGT TGC TC	116 <sup>a</sup>	22-41
	72 <sup>b</sup>	5'-GAC TAT CGG CTT CCC ATT CC	116 <sup>a</sup>	171-190
45	73	5'-CGA TAG AAG CAG CAG GAC AA	116 <sup>a</sup>	575-594
	74 <sup>b</sup>	5'-CTG ATG GAT GCG GAA GAT AC	116 <sup>a</sup>	713-732

<sup>a</sup> Sequences from databases.<sup>b</sup> These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

## Annex VI: Specific and ubiquitous primers for DNA amplification

	SEQ ID NO	Nucleotide sequence	Originating DNA fragment	
			SEQ ID NO	Nucleotide position
<u>Antibiotic resistance gene: vanC</u>				
5	75	5'-GCC TTA TGT ATG AAC AAA TGG	117 <sup>a</sup>	373-393
	76 <sup>b</sup>	5'-GTG ACT TTW GTG ATC CCT TTT GA	117 <sup>a</sup>	541-563
<u>Antibiotic resistance gene: msrA</u>				
10	77	5'-TCC AAT CAT TGC ACA AAA TC	-	-
	78	5'-AAT TCC CTC TAT TTG GTG GT	-	-
<u>Antibiotic resistance gene: satA</u>				
15	79	5'-TCC CAA GCC AGT AAA GCT AA	-	-
	80	5'-TGG TTT TTC AAC TTC TTC CA	-	-
<u>Antibiotic resistance gene: aac(6')-aph(2")</u>				
20	81	5'-TCA TAG AAT GGA TGG CTC AA	-	-
	82	5'-AGC TAC TAT TGC ACC ATC CC	-	-
<u>Antibiotic resistance gene: vat</u>				
25	83	5'-CAA TAA GGG CAT ACC AAA AAT C	-	-
	84	5'-CCT TAA CAT TTG TGG CAT TAT C	-	-
	85	5'-TTG GGA AGA TGA AGT TTT TAG A	-	-
	86	5'-CCT TTA CTC CAA TAA TTT GGC T	-	-
30	<u>Antibiotic resistance gene: vga</u>			
	87	5'-TTT CAT CTA TTC AGG ATG GG	-	-
	88	5'-GGA GCA ACA TTC TTT GTG AC	-	-
35	<u>Antibiotic resistance gene: ermA</u>			
	89	5'-TGT GCC TGA AGA AGG TAT TG	-	-
	90	5'-CGT GTT ACT TCA CCA CCA CT	-	-
40	<u>Antibiotic resistance gene: ermA</u>			
	91	5'-TAT CTT ATC GTT GAG AAG GGA TT	113 <sup>a</sup>	370-392
	92 <sup>b</sup>	5'-CTA CAC TTG GCT TAG GAT GAA A	113 <sup>a</sup>	487-508

45 <sup>a</sup> Sequences from databases.

<sup>b</sup> These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

## Annex VI: Specific and ubiquitous primers for DNA amplification

	SEQ ID NO	Nucleotide sequence	Originating DNA fragment	
			SEQ ID NO	Nucleotide position
<u>Antibiotic resistance gene: ermB</u>				
5	93	5'-CTA TCT GAT TGT TGA AGA AGG ATT	114 <sup>a</sup>	366-389
	94 <sup>b</sup>	5'-GTT TAC TCT TGG TTT AGG ATG AAA	114 <sup>a</sup>	484-507
<u>Antibiotic resistance gene: ermC</u>				
10	95	5'-CTT GTT GAT CAC GAT AAT TTC C	115 <sup>a</sup>	214-235
	96 <sup>b</sup>	5'-ATC TTT TAG CAA ACC CGT ATT C	115 <sup>a</sup>	382-403
<u>Antibiotic resistance gene: meca</u>				
15	97	5'-AAC AGG TGA ATT ATT AGC ACT TGT AAG	-	-
	98	5'-ATT GCT GTT AAT ATT TTT TGA GTT GAA	-	-
<u>Antibiotic resistance gene: int</u>				
20	99	5'-GTG ATC GAA ATC CAG ATC C	-	-
	100	5'-ATC CTC GGT TTT CTG GAA G	-	-
<u>Antibiotic resistance gene: sul</u>				
25	101	5'-CTG GTC ATA CAT GTG ATG G	-	-
	102	5'-GAT GTT ACC CGA GAG CTT G	-	-
<u>Antibiotic resistance gene: sul</u>				
30	103	5'-TTA AGC GTG CAT AAT AAG CC	-	-
	104	5'-TTG CGA TTA CTT CGC CAA CT	-	-
	105	5'-TTT ACT AAG CTT GCC CCT TC	-	-
	106	5'-AAA AGG CAG CAA TTA TGA GC	-	-

35 <sup>a</sup> Sequences from databases.

<sup>b</sup> These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

## SEQUENCE LISTING

## (1) GENERAL INFORMATION:

## (i) APPLICANT:

(A) NAME: INFECTIO DIAGNOSTIC (I.D.I.) INC.

(B) STREET: 2050, BOULEVARD RENE LEVESQUE OUEST, 4E ETAGE

(C) CITY: STE-FOY

(D) STATE: QUEBEC

(E) COUNTRY: CANADA

(F) POSTAL CODE (ZIP): G1V 2K8

(G) TELEPHONE: (418) 681-4343

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(A) NAME: BERGERON, MICHEL G.

(B) STREET: 2069 RUE BRULARD

(C) CITY: SILLERY

(D) STATE: QUEBEC

(E) COUNTRY: CANADA

(F) POSTAL CODE (ZIP): G1T 1G2

(A) NAME: PICARD, FRANCOIS J.

(B) STREET: 1245, RUE DE LA SAPINIERE

(C) CITY: CAP-ROUGE

(D) STATE: QUEBEC

(E) COUNTRY: CANADA

(F) POSTAL CODE (ZIP): G1Y 1A1

(A) NAME: OUELLETTE, MARC

(B) STREET: 1035 DE PLOERMEL

(C) CITY: SILLERY

(D) STATE: QUEBEC

(E) COUNTRY: CANADA

(F) POSTAL CODE (ZIP): G1S 3S1

(A) NAME: ROY, PAUL H.

(B) STREET: 28, RUE CHARLES GARNIER

(C) CITY: LORETTEVILLE

(D) STATE: QUEBEC

(E) COUNTRY: CANADA

(F) POSTAL CODE (ZIP): G2A 3S1

(ii) TITLE OF INVENTION: SPECIES-SPECIFIC, GENUS-SPECIFIC AND  
UNIVERSAL DNA PROBES AND AMPLIFICATION PRIMERS TO RAPIDLY  
DETECT AND IDENTIFY COMMON BACTERIAL AND FUNGAL PATHOGENS  
AND ASSOCIATED ANTIBIOTIC RESISTANCE GENES ...

(iii) NUMBER OF SEQUENCES: 174

(iv) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk

(B) COMPUTER: IBM PC compatible

(C) OPERATING SYSTEM: PC-DOS/MS-DOS

(D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

(vi) PRIOR APPLICATION DATA:

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(A) APPLICATION NUMBER: US 08/743,637  
(B) FILING DATE: 04-NOV-1996

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:  
(A) ORGANISM: *Enterococcus faecium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

TGCTTTAGCA ACAGCCTATC AG

22

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:  
(A) ORGANISM: *Enterococcus faecium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

TAAACTTCTT CCGGCACCTTC G

21

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:  
(A) ORGANISM: *Listeria monocytogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

TGCGGCTATA AATGAAGAGGG C

21

(2) INFORMATION FOR SEQ ID NO: 4:

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- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 21 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: *Listeria monocytogenes*
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

ATCCGATGAT GCTATGGCTT T

21

## (2) INFORMATION FOR SEQ ID NO: 5:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 21 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: *Neisseria meningitidis*
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

CCAGCGGTAT TGTTTGGTGG T

21

## (2) INFORMATION FOR SEQ ID NO: 6:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 21 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: *Neisseria meningitidis*
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

CAGGCGGCCT TTAATAATT C

21

## (2) INFORMATION FOR SEQ ID NO: 7:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 30 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Staphylococcus saprophyticus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

AGATCGAATT CCACATGAAG GTTATTATGA

30

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Staphylococcus saprophyticus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

TCGCTTCTCC CTCAACAATC AAACTATCCT

30

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Streptococcus agalactiae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

TTTCACCAGC TGTATTAGAA GTA

23

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Streptococcus agalactiae*

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

GTTCCCTGAA CATTATCTTT GAT

23

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Candida albicans*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

CAAGAAGGTT GGTTACAACC CAAAGA

26

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Candida albicans*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

AGGTCTTACC AGTAACCTTA CCGGAT

26

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

TACTGACAAA CCATTCATGA TG

22

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs

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- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

AACTTCGTCA CCAACGCGAA C

21

(2) INFORMATION FOR SEQ ID NO: 15:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 20 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

CTGGCGCGGT ATGGTCGGTT

20

(2) INFORMATION FOR SEQ ID NO: 16:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 22 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

GCCGACGTTG GAAGTGGTAA AG

22

(2) INFORMATION FOR SEQ ID NO: 17:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 25 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

CCGTGTTGAA CGTGGTCAAA TCAGA

25

(2) INFORMATION FOR SEQ ID NO: 18:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 25 base pairs

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- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

TRTGTGGTGT RATWGWRCCA GGAGC

25

(2) INFORMATION FOR SEQ ID NO: 19:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 25 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

ACAAACGTGGW CAAGTWTTAG CWGCT

25

(2) INFORMATION FOR SEQ ID NO: 20:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 25 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

ACCATTTCWG TACCTTCTGG TAAGT

25

(2) INFORMATION FOR SEQ ID NO: 21:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 23 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

GAAATTGCAG GNAAATTGAT TGA

23

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(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

TTACGCATGG CNTGACTCAT CAT

23

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:3
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:6
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:9
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:15
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

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ACNKKNACNG GNGTNGARAT GTT

23

## (2) INFORMATION FOR SEQ ID NO: 24:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION: 6
- (D) OTHER INFORMATION:/note= "n = inosine"

## (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION: 9
- (D) OTHER INFORMATION:/note= "n = inosine"

## (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION: 12
- (D) OTHER INFORMATION:/note= "n = inosine"

## (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION: 18
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

AYRTTNTCNC CNGGCATNAC CAT

23

## (2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

TCGCTTCTCC

10

## (2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 600 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Enterococcus faecium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

TTCTTAGAGA CATTGAATAT GCCTTATGTC GGCGCAGGCG TATTGACCAG TGCATGTGCC	60
ATGGATAAAA TCATGACCAA GTATATTAA CAAGCTGCTG GTGTGCCGCA AGTTCCCTTAT	120
GTACCAAGTAC TTAAGAATCA ATGGAAAGAA AATCCTAAAA AAGTATTGAA TCAATGTGAA	180
GGTTCTTGC TTTATCCGAT GTTTGTCAAA CCTGCGAATA TGGGTTCTAG TGTGGCATT	240
ACAAAAGGCAG AAAACCGAGA AGAGCTGCAA AATGCTTAG CAACAGCCTA TCAGTATGAT	300
TCTCGAGCAA TCGTTGAACA AGGAATTGAA GCGCGCGAAA TCGAAGTTGC TGTATTAGGA	360
AATGAAGATG TTCGGACGAC TTTGCCTGGC GAAGTCGTA AAGACGTAGC ATTCTATGAT	420
TATGAAGCCA AATATATCAA TAATAAAATC GAAATGCAGA TTCCAGCCGA AGTGCCGGAA	480
GAAGTTTATC AAAAAGCGCA AGAGTACGCG AAGTTAGCTT ACACGATGTT AGGTGGAAGC	540
GGATTGAGCC GGTGCGATTT CTTTTGACA AATAAAAATG AATTATTCCCT GAATGAATTA	600

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1920 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Listeria monocytogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

GTGGGATTAA ACAGATTTAT GCGTGCGATG ATGGTGGTTT TCATTACTGC CAATTGCATT	60
ACGATTAACC CCGACATAAT ATTTGCAGCG ACAGATAGCG AAGATTCTAG TCTAACACAA	120
GATGAATGGG AAGAAGAAAA AACAGAAGAG CAACCAAGCG AGGTAAATAC GGGACCAAGA	180
TACGAAACTG CACGTGAAGT AAGTTCACGT GATATTAAG AACTAGAAAA ATCGAATAAA	240
GTGAGAAATA CGAACAAAGC AGACCTAATA GCAATGTTGA AAGAAAAAGC AGAAAAAGGT	300
CCAAATATCA ATAATAACAA CAGTGAACAA ACTGAGAATG CGGCTATAAA TGAAGAGGCT	360

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TCAGGAGCCG ACCGACCAGC TATACAAGTG GAGCGTCGTC ATCCAGGATT GCCATCGGAT	420
AGCGCAGCGG AAATTAAGGG AAGAAGGAAA GCCATAGCAT CATCGGATAG TGAGCTTGAA	480
AGCCTTACTT ATCCGGATAA ACCAACAAAA GTAAATAAGA AAAAAGTGGC GAAAGAGTCA	540
GTTGCGGATG CTTCTGAAAG TGACTTAGAT TCTAGCATGC AGTCAGCAGA TGAGTCTTCA	600
CCACAAACCTT TAAAAGCAAA CCAACAACCA TTTTCCCTA AAGTATTTAA AAAAATAAAA	660
GATGCGGGGA AATGGGTACG TGATAAAATC GACGAAAATC CTGAAGTAAA GAAAGCGATT	720
GTTGATAAAA GTGCAGGGTT AATTGACCAA TTATTAACCA AAAAGAAAAG TGAAGAGGTA	780
AATGCTTCGG ACTTCCCGCC ACCACCTACG GATGAAGAGT TAAGACTTGC TTTGCCAGAG	840
ACACCAATGC TTCTTGGTTT TAATGCTCCT GCTACATCAG AACCGAGCTC ATTGAAATT	900
CCACCAACAC CTACGGATGA AGAGTTAAGA CTTGCTTGC CAGAGACGCC AATGCTTCTT	960
GGTTTTAATG CTCCTGCTAC ATCGGAACCG AGCTCGTTCG AATTTCCACC GCCTCCAACA	1020
GAAGATGAAC TAGAAATCAT CCGGGAAACA GCATCCTCGC TAGATTCTAG TTTTACAAGA	1080
GGGGATTTAG CTAGTTGAG AAATGCTATT AATGCCATA GTCAAAATTT CTCTGATTT	1140
CCACCAATCC CAACAGAAGA AGAGTTGAAC GGGAGAGGCG GTAGACCAAC ATCTGAAGAA	1200
TTTAGTTCGC TGAATAGTGG TGATTTACA GATGACGAAA ACAGCGAGAC AACAGAAGAA	1260
GAAATTGATC GCCTAGCTGA TTTAAGAGAT AGAGGAACAG GAAAACACTC AAGAAATGCG	1320
GGTTTTTAC CATTAAATCC GTTTGCTAGC AGCCCGGTTG CTTCGTTAAG TCCAAAGGTA	1380
TCGAAAATAA GCGACCGGGC TCTGATAAGT GACATAACTA AAAAACGCC ATTAAAGAAT	1440
CCATCACAGC CATTAAATGT GTTTAATAAA AAAACTACAA CGAAAACAGT GACTAAAAAA	1500
CCAACCCCTG TAAAGACCGC ACCAAAGCTA GCAGAACTTC CTGCCACAAA ACCACAAGAA	1560
ACCGTACTTA GGGAAAATAA AACACCCATT ATAGAAAAAC AAGCAGAAC AAACAAGCAG	1620
TCAATTAATA TGCCGAGCCT ACCAGTAATC CAAAAAGAAG CTACAGAGAG CGATAAAGAG	1680
GAAATGAAAC CACAAACCGA GGAAAAATG GTAGAGGAAA GCGAATCAGC TAATAACGCA	1740
AACGGAAAAA ATCGTTCTGC TGGCATTGAA GAAGGAAAAC TAATTGCTAA AAGTGCAGAA	1800
GACGAAAAAG CGAAGGAAGA ACCAGGGAAC CATAACGACGT TAATTCTTGC AATGTTAGCT	1860
ATTGGCGTGT TCTCTTCTAGG GGCGTTTATC AAAATTATTC AATTAAGAAA AAATAATTAA	1920

(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 415 base pairs

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Neisseria meningitidis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

TACCGGTACG CTAAATATTG GTGATGTATT GGATATTATG ATTTGGGAAG CGCCGCCAGC	60
GGTATTGTTT GGTGGTGGCC TTTCTTCGAT GGGCTCGGGT AGTGCACAAAC AAACCAAGTT	120
GCCGGAGCAA CTGGTGACGG CACGTGGTAC GGTTTCTGTG CCGTTTGTG GCGATATTC	180
GGTGGTCGGT AAAACGCCTG GTCAGGTTCA GGAAATTATT AAAGGCCGCC TGAAAAAAAT	240
GGCCAATCAG CCGCAAGTGA TGGTGCGCTT GGTGCAGAAT AATGCGCAA ATGTATCGGT	300
GATTGCGCA GGCAATAGTG TGCATGCC GTTGACGGCA GCCGGTGAGC GTGTGTTGGA	360
TGCGGTGGCT GCGGTAGGTG GTTCAACGGC AAATGTGCAG GATACGAATG TGCAG	415

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 438 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Staphylococcus saprophyticus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

TCGCTTCTCC AGAAGAAATT TTAGAAACAT ATCTAGAAAA TCCCAAATTA GATAAACCGT	60
TTATATTATG TGAATACGCA CATGCAATGG GAAATTCAAC AGGAGATCTT AATGCATATC	120
AAACATTAAT TGAAAAATAT GATAGTTTA TTGGCGGTTT TGTTTGGAA TGGTGTGATC	180
ATAGCATTCA GGTTGGATA AAGGAAGGTA AACCAATTT TAGATATGGT GGAGATTTG	240
GTGAGGCCTT ACATGACGGT AATTTTGTTG TTGATGGTAT TGTTTCGCCA GATCGAATTC	300
CACATGAAGG TTATTATGAG TTTAACATG AACATAGACC TTTGAGATTG GTTAACGAAG	360
AGGATTATCG GTTTACATTG AAGAATCAAT TTGATTTAC AAATGCGGAG GATAGTTGA	420
TTGTTGAGGG AGAACGCA	438

## (2) INFORMATION FOR SEQ ID NO: 30:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 768 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus agalactiae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

ATGAACGTTA CACATATGAT GTATCTATCT GGAACCTCTAG TGGCTGGTGC ATTGTTATTT	60
TCACCAGCTG TATTAGAAAGT ACATGCTGAT CAAAGTGACAA CTCCACAAGT GGTAAATCAT	120
GTAAAATAGTA ATAATCAAGC CCAGCAAATG GCTCAAAAGC TTGATCAAGA TAGCATTGAG	180
TTGAGAAATA TCAAAGATAA TGTTCAGGGA ACAGATTATG AAAAACCGGT TAATGAGGCT	240
ATTACTAGCG TGGAAAAATT AAAGACTTCA TTGCGTGCCA ACCCTGAGAC AGTTTATGAT	300
TTGAATTCTA TTGGTAGTCG TGTAGAAGCC TTAACAGATG TGATTGAAGC AATCACTTT	360
TCAACTCAAC ATTTAACAAA TAAGGTTAGT CAAGCAAATA TTGATATGGG ATTTGGGATA	420
ACTAAGCTAG TTATTCGCAT TTTAGATCCA TTTGCTTCAG TTGATTCAAT TAAAGCTCAA	480
GTAAACGATG TAAAGGCATT AGAACAAAAA GTTTAACTT ATCCTGATTT AAAACCAACT	540
GATAGAGCTA CCATCTATAC AAAATCAAAA CTTGATAAGG AAATCTGGAA TACACGCTTT	600
ACTAGAGATA AAAAAGTACT TAACGTAAA GAATTAAAG TTTACAATAC TTTAAATAAA	660
GCAATCACAC ATGCTGTTGG AGTTCAAGTTG AATCCAAATG TTACGGTACA ACAAGTTGAT	720
CAAGAGATTG TAACATTACA AGCAGCACTT CAAACAGCAT TAAAATAA	768

## (2) INFORMATION FOR SEQ ID NO: 31:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 421 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Neisseria meningitidis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

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ATGAAAGTAG GTTTCGTCGG CTGGCGCGGT ATGGTCGGTT CGGTTTGAT GCAGCGTATG	60
AAAGAAGAAA ACGACTTCGC CCACATTCCC GAAGCGTTT TCTTTACAC TTCCAACGTC	120
GGCGGCGCAC GCCCTGATTT CGGTCAGGCG GCTAAAACAT TATTGGACGC GAACAAACGTT	180
GCCGAGCTGG CAAAAATGGA CATCATCGTT ACCTGCCAAG GCGGCGACTA CACCAAATCC	240
GTCTTCCAAG CCCTGCGCGA CAGCGGCTGG AACGGCTACT GGATTGACGC GGCATCCTCG	300
CTGCGTATGA AAGACGACGC GATTATCGTC CTCGACCCCG TCAACCGCAA CGTCATCGAC	360
AACGGCCTCA AAAACGGCGT GAAAAAACTAC ATCGGCGGCA ACTGTACCGT TTCCCTGATG	420
C	421

## (2) INFORMATION FOR SEQ ID NO: 32:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 213 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus gordonii*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

TTCATAGACG CTGAGCACGC TTTGGATCCA TCTTACGCGG CTGCTCTAGG TGTAAATATT	60
GATGAGCTGT TGCTATCTCA ACCAGATTCT GGTGAGCAAG GTTTAGAAAT TGCAGGAAAA	120
TTGATTGACT CTGGGGCAGT TGATTTAGTT GTCATCGACT CTGTTGCAGC TCTTGTACCA	180
CGTGCAGAAA TCGATGGAGA TATCGGTGAT AGC	213

## (2) INFORMATION FOR SEQ ID NO: 33:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 692 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus mutans*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

GGGCCGGAAAT CTTCTGGTAA GACAACTGTC GCTCTTCATG CTGCTGCTCA GGCGAAAAAA	60
--	----

GATGGCGGTA TTGCCGCTTT CATTGATGCA GAACATGCC CTTGATCCAGC CTATGCTGCT	120
GCTCTTGGCG TTAATATTGA TGAGCTTTG CTTTCACAAAC CAGATTCAAG AGAACAGGGT	180
CTTGAAATTG CAGGGAAATT GATTGATTCT GGCGCTGTTG ATTTAGTTGT TGTTGACTCA	240
GTGGCAGCTT TAGTACCAACG TGCGGAGATT GACGGAGATA TTGGTAATAG TCATGTTGGC	300
TTACAAGCAC GCATGATGAG TCAAGCGATG CGTAAATTAT CAGCTTCAAT CAATAAAACA	360
AAAACCATTG CTATTTTAT TAATCAATTG CGGGAAAAAG TTGGTATTAT GTTTGGTAAT	420
CCAGAAACAA CCCCTGGCGG GCGTGCCTTG AAGTTTATT CTTCTGTGCG TCTTGATGTC	480
CGCGGCAATA CTCAAATTAA AGGAACCGGG GAACAAAAAG ACAGCAATAT TGGTAAAGAG	540
ACCAAAATTA AAGTTGTTAA AAATAAAGTT GCTCCACCAT TTAAGGAAGC TTTTGTAGAA	600
ATTATATATG GTGAAGGCAT TTCTCGTACA GGTGAATTAG TTAAGATTGC CAGTGATTTG	660
GGAATTATCC AAAAGCTGG AGCTTGGTAC TC	692

## (2) INFORMATION FOR SEQ ID NO: 34:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1204 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus pneumoniae*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

ATGGCGAAAA AACCAAAAAA ATTAGAAGAA ATTTCAAAAA AATTGGGGC AGAACGTGAA	60
AAGGCCTTGA ATGACGCTCT TAAATTGATT GAGAAAGACT TTGGTAAAGG ATCAATCATG	120
CGTTTGGGTG AACGTGCGGA GCAAAAGGTG CAAGTGATGA GCTCAGGTTTC TTTAGCTCTT	180
GACATTGCC C TTGGCTCAGG TGGTTATCCT AAGGGACGTA TCATCGAAAT CTATGGCCCA	240
GAGTCATCTG GTAAGACAAC GGTTGCCCTT CATGCAGTTG CACAAGCGCA AAAAGAAGGT	300
GGGATTGCTG CCTTTATCGA TGCGGAACAT GCCCTTGATC CAGCTTATGC TGCGGCCCTT	360
GGTGTCAATA TTGACGAATT GCTCTTGTCT CAACCAGACT CAGGAGAGCA AGGTCTTGAG	420
ATTGCGGGAA AATTGATTGA CTCAGGTGCA GTTGATCTTG TCGTAGTCGA CTCAGTTGCT	480
GCCCTTGTTC CTCGTGCGGA AATTGATGGA GATATCGGAG ATAGCCATGT TGGTTGCAG	540
GCTCGTATGA TGAGCCAGGC CATGCGTAAA CTTGGCGCCT CTATCAATAA AACCAAAACA	600

ATTGCCATTT TTATCAACCA ATTGCGTGAA AAAGTTGGAG TGATGTTGG AAATCCAGAA	660
ACAACACCGG CGGGACGTGC TTTGAAATTC TATGCTTCAG TCCGCTTGGA TGTCGTGGT	720
AATAACACAAA TTAAGGGAAC TGGTGATCAA AAAGAAACCA ATGTCGGTAA AGAAACTAAG	780
ATTAAGGTTG TAAAAAATAA GGTAGCTCCA CCGTTAAGG AAGCCGTAGT TGAAATTATG	840
TACGGAGAAG GAATTTCTAA GACTGGTGAG CTTTGAAAGA TTGCAAGCGA TTTGGATATT	900
ATCAAAAAAG CAGGGGCTTG GTATTCTTAC AAAGATGAAA AAATTGGCA AGGTTCTGAG	960
AATGCTAAGA AATACTTGGC AGAGCACCCA GAAATCTTG ATGAAATTGA TAAGCAAGTC	1020
CGTTCTAAAT TTGGCTTGAT TGATGGAGAA GAAGTTTCAG AACAAAGATAC TGAAAACAAA	1080
AAAGATGAGC CAAAGAAAGA AGAACAGTG AATGAAGAAG TTCCGCTTGA CTTAGGCGAT	1140
GAACATTGAAA TCGAAATTGA AGAATAAGCT GTTAAAGCAG TGGAGAAATC CGCTACTTTT	1200
TCGA	1204

## (2) INFORMATION FOR SEQ ID NO: 35:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 981 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus pyogenes*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

ATGCGTTCAAG GAAAGTCTAGC TCTTGATATT GCTTGGATAG CTGGTGGTTA TCCTAAAGGA	60
CGTATCATCG AAATCTATGG TCCAGAGTCT TCCGGTAAAA CGACTGTGGC TTTACATGCT	120
GTAGCACAAG CTCAAAAAGA AGGTGGAATC GCAGCCTTTA TCGATGCCGA GCATGCGCTT	180
GATCCAGCTT ATGCTGCTGC GCTTGGGGTT AATATTGATG AACTTCTCTT GTCTCAACCA	240
GATTCTGGAG AACAAAGGACT TGAAATTGCA GGTAAATTGA TTGATTCTGG TGCGGTTGAC	300
CTGGTTGTTG TCGATTCACT AGCAGCTTTA GTGCCACGTG CTGAAATTGA TGGTGTGATATT	360
GGCGATAGCC ATGTCGGATT GCAAGCACGT ATGATGAGTC AGGCCATGCG TAAATTATCA	420
GCTTCTATTA ATAAAAACAAA AACTATCGCA ATCTTATCA ACCAATTGCG TGAAAAAGTT	480
GGTGTGATGT TTGGAAATCC TGAAACAAACA CCAGGTGGTC GAGCTTGAA ATTCTATGCT	540
TCTGTTCGGC TGGATGTGCG TGGAAACAAAC CAAATTAAAG GAACTGGTGA CCAAAAGATA	600

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GCCAGCATTG GTAAGGAGAC CAAAATCAAG GTTGTAAAAA ACAAGGTCGC TCCGCCATTT	660
AAGGTAGCAG AAGTTGAAAT CATGTATGGG GAAGGTATTT CTCGTACAGG GGAGCTTGTG	720
AAAATTGCTT CTGATTTGGA CATTATCCAA AAAGCAGGTG CTTGGTTCTC TTATAATGGT	780
GAGAAGATTG GCCAAGGTTC TGAAAATGCT AAGCGTTATT TGGCCGATCA TCCACAATTG	840
TTTGATGAAA TCGACCGTAA AGTACGTGTT AAATTTGGTT TGCTTGAAGA AAGCGAAGAA	900
GAATCTGCTA TGGCAGTAGC ATCAGAAGAA ACCGATGATC TTGCTTTAGA TTTAGATAAT	960
GGTATTGAAA TTGAAGATTA A	981

## (2) INFORMATION FOR SEQ ID NO: 36:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 312 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus salivarius*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

GCGTATGCAC GAGCTCTAGG TGTAAATATC GATGAGCTTC TTTTGTGCA GCCTGATTCT	60
GGTGAGCAAG GTCTCGAAAT TGCAGGTAAG CTGATTGACT CTGGTGCAGT GGATTTAGTT	120
GTTGTTGACT CAGTTGCGGC CTTCGTACCA CGTGCAGAAA TTGATGGAGA TAGTGGTGAC	180
AGTCATGTAG GACTTCAAGC GCGTATGATG AGTCAAGCCA TGC GTAAACT TTCTGCATCT	240
ATTAATAAAA CAAAAACGAT TGCTATCTTT ATTAACCAGT TGC GTGAAAAGTTGGTATC	300
ATGTTTGGTA AC	312

## (2) INFORMATION FOR SEQ ID NO: 37:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

CTATGTGGCG CGGTATTATC	20
-----------------------	----

## (2) INFORMATION FOR SEQ ID NO: 38:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

CGCAGTGTAA TCACATCATGG

20

(2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

CTGAATGAAG CCATACCAAA

20

(2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

ATCAGCAATA AACCAAGCCAG

20

(2) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

TTACCATGAG CGATAAACAGC

20

(2) INFORMATION FOR SEQ ID NO: 42:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

CTCATTCA GT TCCGTTCCCC

20

(2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

CAGCTGCTGC AGTGGATGGT

20

(2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

CGCTCTGCTT TGTTATTCCGG

20

(2) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

TACGCCAAC A TCGTGGAAAG

20

(2) INFORMATION FOR SEQ ID NO: 46:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

TTGAATTTGG CTTCTTCGGT

20

(2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

GGGATACAGA AACGGGACAT

20

(2) INFORMATION FOR SEQ ID NO: 48:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

TAAATCTTT TCAGGCAGCG

20

(2) INFORMATION FOR SEQ ID NO: 49:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 25 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

GATGGTTTGA AGGGTTTATT ATAAG

25

(2) INFORMATION FOR SEQ ID NO: 50:

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(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 25 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

AATTTAGTGT GTTTAGAATG GTGAT

25

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 21 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

ACTTCAACAC CTGCTGCTTT C

21

(2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 21 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

TGACCACCTT TATCAGCAAC C

21

(2) INFORMATION FOR SEQ ID NO: 53:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 20 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

GGCAATAGTT GAAATGCTCG

20

(2) INFORMATION FOR SEQ ID NO: 54:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

CAGCTGTTAC AACGGACTGG

20

(2) INFORMATION FOR SEQ ID NO: 55:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

TCTATGATCT CGCAGTCTCC

20

(2) INFORMATION FOR SEQ ID NO: 56:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

ATCGTCACCG TAATCTGCTT

20

(2) INFORMATION FOR SEQ ID NO: 57:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

CATTCTCGAT TGCTTGCTA

20

(2) INFORMATION FOR SEQ ID NO: 58:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

CCGAAATGCT TCTCAAGATA

20

(2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

CTGGATTATG GCTACGGAGT

20

(2) INFORMATION FOR SEQ ID NO: 60:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

AGCAGTGTGA TGGTATCCAG

20

(2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

GACTCTTGAT GAAGTGCTGG

20

(2) INFORMATION FOR SEQ ID NO: 62:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:

CTGGTCTATT CCTCGCACTC

20

(2) INFORMATION FOR SEQ ID NO: 63:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

TATGAGAAGG CAGGATT CGT

20

(2) INFORMATION FOR SEQ ID NO: 64:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:

GCTTTCTCTC GAAGGCTT GT

20

(2) INFORMATION FOR SEQ ID NO: 65:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

GAGTTGCTGT TCAATGATCC

20

(2) INFORMATION FOR SEQ ID NO: 66:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

GTGTTTGAAC CATGTACACG

20

(2) INFORMATION FOR SEQ ID NO: 67:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

TGTAGAGGTC TAGCCCGTGT

20

(2) INFORMATION FOR SEQ ID NO: 68:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

ACGGGGATAA CGACTGTATG

20

(2) INFORMATION FOR SEQ ID NO: 69:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

ATAAAGATGA TAGGCCGGTG

20

(2) INFORMATION FOR SEQ ID NO: 70:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

TGCTGTCATA TTGTCTTGCC

20

(2) INFORMATION FOR SEQ ID NO: 71:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

ATTATCTTCG GCGGTTGCTC

20

(2) INFORMATION FOR SEQ ID NO: 72:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

GACTATCGGC TTCCCCATTCC

20

(2) INFORMATION FOR SEQ ID NO: 73:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

CGATAGAACG AGCAGGGACAA

20

(2) INFORMATION FOR SEQ ID NO: 74:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

CTGATGGATG CGGAAGATA

20

(2) INFORMATION FOR SEQ ID NO: 75:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:

GCCTTATGTA TGAACAAATG G

21

(2) INFORMATION FOR SEQ ID NO: 76:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

GTGACTTTWG TGATCCCTTT TGA

23

(2) INFORMATION FOR SEQ ID NO: 77:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

TCCAATCATT GCACAAAATC

20

(2) INFORMATION FOR SEQ ID NO: 78:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

AATTCCCTCT ATTTGGTGGT

20

(2) INFORMATION FOR SEQ ID NO: 79:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

TCCAAGCCA GTAAAGCTAA

20

(2) INFORMATION FOR SEQ ID NO: 80:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

TGGTTTTCA ACTTCTTCCA

20

(2) INFORMATION FOR SEQ ID NO: 81:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

TCATAGAATG GATGGCTCAA

20

(2) INFORMATION FOR SEQ ID NO: 82:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

AGCTACTATT GCACCATCCC

20

(2) INFORMATION FOR SEQ ID NO: 83:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

CAATAAGGGC ATACCAAAAA TC

22

(2) INFORMATION FOR SEQ ID NO: 84:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

CCTTAACATT TGTGGCATT A TC

22

(2) INFORMATION FOR SEQ ID NO: 85:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

TTGGGAAGAT GAAGTTTTA GA

22

(2) INFORMATION FOR SEQ ID NO: 86:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

CCTTTACTCC AATAATTTGG CT

22

(2) INFORMATION FOR SEQ ID NO: 87:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

TTTCATCTAT TCAGGATGGG

20

(2) INFORMATION FOR SEQ ID NO: 88:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

GGAGCAACAT TCTTGATGAC

20

(2) INFORMATION FOR SEQ ID NO: 89:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:

TGTGCCTGAA GAAGGTATTG

20

(2) INFORMATION FOR SEQ ID NO: 90:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

CGTGTTACTT CACCACCACT

20

(2) INFORMATION FOR SEQ ID NO: 91:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

TATCTTATCG TTGAGAAGGG ATT

23

(2) INFORMATION FOR SEQ ID NO: 92:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

CTACACTTGG CTTAGGATGA AA

22

(2) INFORMATION FOR SEQ ID NO: 93:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 24 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:

CTATCTGATT GTTGAAGAAG GATT

24

(2) INFORMATION FOR SEQ ID NO: 94:

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(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 24 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:

GTTTACTCTT GGTTTAGGAT GAAA

24

(2) INFORMATION FOR SEQ ID NO: 95:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 22 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

CTTGTTGATC ACGATAATTT CC

22

(2) INFORMATION FOR SEQ ID NO: 96:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 22 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

ATCTTTAGC AAACCCGTAT TC

22

(2) INFORMATION FOR SEQ ID NO: 97:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 27 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

AACAGGTGAA TTATTAGCAC TTGTAAG

27

(2) INFORMATION FOR SEQ ID NO: 98:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 27 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

ATTGCTGTTA ATATTTTTG AGTTGAA

27

(2) INFORMATION FOR SEQ ID NO: 99:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 19 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:

GTGATCGAAA TCCAGATCC

19

(2) INFORMATION FOR SEQ ID NO: 100:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 19 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:

ATCCTCGGTT TTCTGGAAG

19

(2) INFORMATION FOR SEQ ID NO: 101:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 19 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101:

CTGGTCATAC ATGTGATGG

19

(2) INFORMATION FOR SEQ ID NO: 102:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 19 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:

GATGTTACCC GAGAGCTTG

19

(2) INFORMATION FOR SEQ ID NO: 103:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:

TTAAGCGTGC ATAATAAGCC

20

(2) INFORMATION FOR SEQ ID NO: 104:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:

TTGCGATTAC TTTCGCCAACT

20

(2) INFORMATION FOR SEQ ID NO: 105:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:

TTTACTAAGC TTGCCCCCTTC

20

(2) INFORMATION FOR SEQ ID NO: 106:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

AAAAGGCAGC AATTATGAGC

20

(2) INFORMATION FOR SEQ ID NO: 107:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 29 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:9
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:15
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:18
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:21
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:

AAYATGATNA CNGGNGCNGC NCARATGGA

29

(2) INFORMATION FOR SEQ ID NO: 108:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid

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- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:3
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:6
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:9
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:

CCNACNGTNC KNCCRCCYTC RCG

23

(2) INFORMATION FOR SEQ ID NO: 109:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 29 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:6
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:15
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature

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(B) LOCATION:18  
 (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

CARYTNATHG TNGCNGTNAA YAARATGGA

29

(2) INFORMATION FOR SEQ ID NO: 110:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 831 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

ATGAAAAACA CAATACATAT CAACTTCGCT ATTTTTTAA TAATTGAAA TATTATCTAC	60
AGCAGCGCCA GTGCATCAAC AGATATCTCT ACTGTTGCAT CTCCATTATT TGAAGGAACT	120
GAAGGTTGTT TTTTACTTTA CGATGCATCC ACAAAACGCTG AAATTGCTCA ATTCAATAAA	180
GCAAAAGTGTG CAACGCAAAT GGCACCAGAT TCAACTTCA AGATCGCATT ATCACTTATG	240
GCATTTGATG CGGAAATAAT AGATCAGAAA ACCATATTCA AATGGGATAA AACCCCCAAA	300
GGAATGGAGA TCTGGAACAG CAATCATACA CCAAAGACGT GGATGCAATT TTCTGTTGTT	360
TGGGTTTCGC AAGAAATAAC CCAAAAAATT AGATTAATAA AAATCAAGAA TTATCTCAAA	420
GATTTTGATT ATGGAAATCA AGACTTCTCT GGAGATAAAG AAAGAAACAA CGGATTAACA	480
GAAGCATGGC TCGAAAGTAG CTTAAAAATT TCACCAGAAG AACAAATTCA ATTCCCTGCGT	540
AAAATTATTA ATCACAATCT CCCAGTTAAA AACTCAGCCA TAGAAAACAC CATAGAGAAC	600
ATGTATCTAC AAGATCTGGA TAATAGTACA AAAACTGTATG GGAAAACGTG TGCAGGATTC	660
ACAGCAAATA GAACCTTACA AAACGGATGG TTTGAAGGGT TTATTATAAG CAAATCAGGA	720
CATAAAATATG TTTTTGTGTC CGCACTTACA GGAAAACGTGG GGTCGAATT AACATCAAGC	780
ATAAAAGCCA AGAAAAATGC GATCACCATT CTAAACACAC TAAATTATA A	831

(2) INFORMATION FOR SEQ ID NO: 111:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 846 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:

TTGAAAAAGT TAATATTTT AATTGTAATT GCTTAGTTT TAAGTGCATG TAATTCAAAC	60
AGTTCACATG CCAAAGAGTT AAATGATTAA GAAAAAAAAT ATAATGCTCA TATTGGTGT	120
TATGCTTAGT ATACTAAAAG TGGTAAGGAA GTAAAATTAA ATTCAGATAA GAGATTGCC	180
TATGCTTCAA CTTCAAAAGC GATAAAATAGT GCTATTTGT TAGAACAAAGT ACCTTATAAT	240
AAGTTAAATA AAAAAGTACA TATTAACAAA GATGATATAG TTGCTTATTC TCCTATTTA	300
GAAAAATATG TAGGAAAAGA TATCACTTAA AAAGCACTTA TTGAGGCTTC AATGACATAT	360
AGTGATAATA CAGCAAACAA TAAAATTATA AAAGAAATCG GTGGAATCAA AAAAGTTAAA	420
CAACGTCTAA AAGAACTAGG AGATAAAAGTA ACAAAATCCAG TTAGATATGA GATAGAATTA	480
AATTACTATT CACCAAAGAG CAAAAAAGAT ACTTCAACAC CTGCTGCTT CGGTAAGACT	540
TTAAATAAAC TTATCGAAA TGGAAAATTAA AGCAAAGAAA ACAAAAAATT CTTACTTGAT	600
TTAATGTTAA ATAATAAAAG CGGAGATACT TTAATTAAAG ACGGTGTTCC AAAAGACTAT	660
AAGGTTGCTG ATAAAAGTGG TCAAGCAATA ACATATGCTT CTAGAAATGA TGTTGCTTT	720
GTTCATCCTA AGGGCCAATC TGAACCTATT GTTTAGTCA TTTTACGAA TAAAGACAAT	780
AAAAGTGATA AGCCAAATGA TAAGTTGATA AGTCAAACCG CCAAGAGTGT AATGAAGGAA	840
TTTTAA	846

## (2) INFORMATION FOR SEQ ID NO: 112:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 555 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:

ATGTCCGCGA GCACCCCCC CATAACTCTT CGCCTCATGA CCGAGCGCGA CCTGCCGATG	60
CTCCATGACT GGCTCAACCG GCCGCACATC GTTGAGTGGT GGGGTGGCGA CGAAGAGCGA	120
CCGACTCTTG ATGAAAGTGC GGAACACTAC CTGCCAGAG CGATGGCGGA AGAGTCCGTA	180
ACACCGTACA TCGCAATGCT GGGCGAGGAA CCGATCGGCT ATGCTCAGTC GTACGTCGCG	240
CTCGGAAGCG GTGATGGCTG GTGGGAAGAT GAAACTGATC CAGGAGTGCAG AGGAATAGAC	300
CAGTCTCTGG CTGACCCGAC ACAGTTGAAC AAAGGCCTAG GAACAAGGCT TGTCCCGCGCT	360

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CTCGTTGAAC TACTGTTCTC GGACCCCACC GTGACGAAGA TTCAGACCGA CCCGACTCCG	420
AACAACCATC GAGCCATACG CTGCTATGAG AAGGCAGGAT TCGTGCAGGA GAAGATCATC	480
ACCACGCCTG ACGGGCCGGC GGTTTACATG GTTCAAACAC GACAAGCCTT CGAGAGAAAG	540
CGCGGTGTTG CCTAA	555

(2) INFORMATION FOR SEQ ID NO: 113:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 732 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

ATGAACCAGA AAAACCCCTAA AGACACGCAA AATTTTATTA CTTCTAAAAA GCATGTAAAA	60
GAAATATTGA ATCACACGAA TATCAGTAAA CAAGACAACG TAATAGAAAT CGGATCAGGA	120
AAAGGACATT TTACCAAAGA GCTAGTCAAA ATGAGTCGAT CAGTTACTGC TATAGAAATT	180
GATGGAGGCT TATGTCAAGT GACTAAAGAA GCGGTAAACC CCTCTGAGAA TATAAAAGTG	240
ATTCAAACGG ATATTCTAAA ATTTCCCTTC CCAAAACATA TAAACTATAA GATATATGGT	300
AATATTCCCTT ATAACATCAG TACGGATATT GTCAAAAGAA TTACCTTGA AAGTCAGGCT	360
AAATATAGCT ATCTTATCGT TGAGAAGGGA TTTGCGAAAA GATTGCAAAA TCTGCAACGA	420
GCTTTGGGTT TACTATTAAT GGTGGAGATG GATATAAAA TGCTCAAAA AGTACCACCA	480
CTATATTTTC ATCCTAAGCC AAGTGTAGAC TCTGTATTGA TTGTTCTTGA ACGACATCAA	540
CCATTGATT CAAGAAGGA CTACAAAAAG TATCGATCTT TTGTTTATAA GTGGGTAAAC	600
CGTGAATATC GTGTTCTTTT CACTAAAAAC CAATTCCGAC AGGCTTGAA GCATGCAAAT	660
GTCACTAATA TTAATAAACT ATCGAAGGAA CAATTCTTT CTATTTCAA TAGTTACAAA	720
TTGTTTCACT AA	732

(2) INFORMATION FOR SEQ ID NO: 114:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 738 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

ATGAACAAAA ATATAAAATA TTCTCAAAAC TTTTTAACGA GTGAAAAAGT ACTCAACCAA	60
ATAATAAAAC AATTGAATT T AAAAGAAACC GATACCGTTT ACGAAATTGG AACAGGTAAA	120
GGGCATTTAA CGACGAAACT GGCTAAAATA AGTAAACAGG TAACGTCTAT TGAATTAGAC	180
AGTCATCTAT TCAACTTATC GTCAGAAAAA TTAAAATCGA ATACTCGTGT CACTTTAATT	240
CACCAAGATA TTCTACAGTT TCAATTCCCT AACAAACAGA GGTATAAAAT TGTTGGGAAT	300
ATTCCTTACC ATTTAAGCAC ACAAAATTATT AAAAAAGTGG TTTTGAAAG CCATGCGTCT	360
GACATCTATC TGATTGTTGA AGAAGGATTTC TACAAGCGTA CCTTGGATAT TCACCGAACAA	420
CTAGGGTTGC TCTTGCACAC TCAAGTCTCG ATTCAAGCAAT TGCTTAAGCT GCCAGCGGAA	480
TGCTTCATC CTAAACCAAG AGTAAACAGT GTCTTAATAA AACTTACCCG CCATACCCACA	540
GATGTTCCAG ATAAATATTG GAAGCTATAT ACGTACTTTG TTTCAAAATG GGTCAATCGA	600
GAATATCGTC AACTGTTTAC TAAAAATCAG TTTCATCAAG CAATGAAACA CGCCAAAGTA	660
AACAATTAA GTACCGTTAC TTATGAGCAA GTATTGTCTA TTTTTAATAG TTATCTATTA	720
TTAACGGGA GGAAATAA	738

## (2) INFORMATION FOR SEQ ID NO: 115:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 735 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

ATGAACGAGA AAAATATAAA ACACAGTCAA AACTTTATTA CTTCAAAACA TAATATAGAT	60
AAAATAATGA CAAATATAAG ATTAAATGAA CATGATAATA TCTTTGAAAT CGGCTCAGGA	120
AAAGGGCATT TTACCCCTTGA ATTAGTACAG AGGTGTAATT TCGTAACTGC CATTGAAATA	180
GACCATAAAAT TATGCAAAAC TACAGAAAAT AAACTTGTG ATCACGATAA TTTCCAAGTT	240
TTAAACAAAGG ATATATTGCA GTTTAAATT CCTAAAAACC AATCCTATAA AATATTTGGT	300
AATATACCTT ATAACATAAG TACGGATATA ATACGAAAA TTGTTTTGA TAGTATAGCT	360
GATGAGAGTT ATTTAACCGT GGAATACGGG TTTGCTAAAA GATTATTAAA TACAAACGC	420
TCATTGGCAT TATTTTAAT GGCAGAAGTT GATATTCTA TATTAAGTAT GGTTCCAAGA	480

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GAATATTTTC ATCCTAAACC TAGAGTGAAT AGCTCACTTA TCAGATTAAA TAGAAAAAAA	540
TCAAGAATAT CACACAAAGA TAAACAGAAG TATAATTATT TCGTTATGAA ATGGGTTAAC	600
AAAGAATACA AGAAAATATT TACAAAAAAT CAATTTAACCA ATTCCCTTAAA ACATGCAGGA	660
ATTGACGATT TAAACAATAT TAGCTTGAA CAATTCTTAT CTCTTTCAA TAGCTATAAA	720
TTATTTAATA AGTAA	735

## (2) INFORMATION FOR SEQ ID NO: 116:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1029 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

ATGAATAAAA TAAAAGTCGC AATTATCTTC GGCGGTTGCT CGGAGGAACA TGATGTGTCG	60
GTAAAATCCG CAATAGAAAAT TGCTGCGAAC ATTAATACTG AAAAATTGAA TCCGCACTAC	120
ATCGGAATTA CAAAAAACGG CGTATGGAAG CTATGCAAGA AGCCATGTAC GGAATGGGAA	180
GCCGATAGTC TCCCCGCCAT ATTCTCCCCG GATAGGAAAA CGCATGGTCT GCTTGTCA	240
AAAGAAAGAG AATACGAAAC TCGGCGTATT GACGTGGCTT TCCCGGTTTT GCATGGCAA	300
TGCGGGGAGG ATGGTGCAT ACAGGGTCTG TTTGAATTGT CTGGTATCCC CTATGTAGGC	360
TGCGATATTC AAAGCTCCGC AGCTTGCATG GACAAATCAC TGGCCTACAT TCTTACAAA	420
AATGCGGGCA TCGCCGTCCC CGAATTCAA ATGATTGAAA AAGGTGACAA ACCGGAGGCG	480
AGGACGCTTA CCTACCCCTGT CTTTGTGAAG CGGGCACGGT CAGGTTCGTC CTTTGGCGTA	540
ACCAAAGTAA ACAGTACGGA AGAACTAAC GCTGCGATAG AAGCAGCAGG ACAATATGAT	600
GGAAAAATCT TAATTGAGCA AGCGATTTCG GGCTGTGAGG TCGGCTGCGC GGTCA	660
AACGAGGATG ATTTGATTGT CGGCGAAGTG GATCAAATCC GGTTGAGCCA CGGTATCTTC	720
CGCATCCATC AGGAAAACGA GCCGGAAAAA GGCTCAGAGA ATGCGATGAT TATCGTTCCA	780
GCAGACATTC CGGTCGAGGA ACGAAATCGG GTGCAAGAAA CGGCAAAGAA AGTATATCGG	840
GTGCTTGGAT GCAGAGGGCT TGCTCGTGT GATTTTTTT TGCAGGAGGA TGGCGGCATC	900
TTTCTAAACG AGGTCAATAC CCTGCCCGGT TTTACATCGT ACAGCCGCTA TCCACGCATG	960
GCGGCTGCCG CAGGAATCAC GCTTCCCGCA CTAATTGACA GCCTGATTAC ATTGGCGATA	1020

GAGAGGTGA

1029

## (2) INFORMATION FOR SEQ ID NO: 117:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1031 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

ATGAAAAAAA TTGCCGTTT ATTGGAGGG AATTCTCCAG AATACTCAGT GTCACTAAC	60
TCAGCAGCAA GTGTGATCCA AGCTATTGAC CCGCTGAAAT ATGAAGTAAT GACCATTGGC	120
ATCGCACCAA CAATGGATTG GTATTGGTAT CAAGGAAACC TCGCGAATGT TCGCAATGAT	180
ACTTGGCTAG AAGATCACAA AAACTGTCAC CAGCTGACTT TTTCTAGCCA AGGATTTATA	240
TTAGGAGAAA AACGAATCGT CCCTGATGTC CTCTTCCAG TCTTGCATGG GAAGTATGGC	300
GAGGATGGCT GTATCCAAGG ACTGCTTGAA CTAATGAACC TGCCTTATGT TGGTTGCCAT	360
GTCGCTGCCT CCGCATTATG TATGAACAAA TGGCTTTGC ATCAACTTGC TGATACCATG	420
GGAATCGCTA GTGCTCCAC TTTGCTTTA TCCCGCTATG AAAACGATCC TGCCACAATC	480
GATCGTTTA TTCAAGACCA TGGATTCCCG ATCTTATCA AGCCGAATGA AGCCGGTTCT	540
TCAAAAGGGA TCACAAAAGT AACTGACAAA ACAGCGCTCC AATCTGCATT AACGACTGCT	600
TTTGCTTACG GTTCTACTGT GTTGATCCAA AAGGGCGATAG CGGGTATTGA AATTGGCTGC	660
GGCATCTTAG GAAATGAGCA ATTGACGATT GGTGCTTGTG ATGCGATTTC TCTTGTGAC	720
GGTTTTTTTG ATTTGAAGA GAAATACCAA TTAATCAGCG CCACGATCAC TGTCCCAGCA	780
CCATTGCCTC TCGCGCTTGA ATCACAGATC AAGGAGCAGG CACAGCTGCT TTATCGAAC	840
TTGGGATTGA CGGGCTGGC TCGAATCGAT TTTTCGTCA CCAATCAAGG AGCGATTTAT	900
TTAAACGAAA TCAACACCAT GCCGGGATT ACTGGGCACT CCCGCTACCC AGCTATGATG	960
GCGGAAGTCG GGTTATCCTA CGAAATATTA GTAGAGCAAT TGATTGCACT GGCAGAGGAG	1020
GACAAACGAT G	1031

## (2) INFORMATION FOR SEQ ID NO: 118:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 809 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Abiotrophia adiacens*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

TGGTGCTATC TTAGTAGTAT CTGCAGCTGA TGGTCCAATG CCTCAACAC	60
CTTATTATCA CGTCAAGTAG GTGTTCTTA CATCGTTGA TTCTTAAACA	120
AAGTTGACAT GGTTGACGAT GAAGAATTAT TAGAATTAGT AGAAATGGAA GTTCGTGACT	180
TATTATCAGA ATACGATTC CCAGGCATG ACACTCCAGT TGTTGCAGGT TCTGCTTAC	240
GCGCTTTAGA AGGCGACGCT TCATACRAAG AAAAAATCTT AGAATTAAATG GCTGCTGTTG	300
ACGAATACAT TCCAACCTCA GAACGYGACG TTGACAAACC ATTCAATGATG CCAGTTGAAG	360
ACGTGTTCTC AATCACAGGT CGTGGTACTG TTGCTACAGG TCGTGTGAA CGTGGACAAG	420
TTCGTGTGAG TGACGAAGTT GAAATCGTTG GTATTCAGA AGAAACTTCA AAAACAAC	480
ACTG TGTTGTGTT ACACGTGACA ACATCGAACG TGGACAAGTT CTTGCTAAC	540
CAGGAACAAAT CACTCCACAT ACTAAATTCA AAGCTGAAGT TTACGTATTA ACTAAAGAAG	600
AAGGTGGACG TCATACTCCA TTCTTCTCTA ACTACCGTCC TCAATTCTAC TTCCGTACAA	660
CAGACATCAC TGGTGTGTT GTGTTACCAAG AAGGCAGTTGA AATGGTAATG CCTGGTGATA	720
ACGTAACATAT GGAAGTTGAA TTAATTCAACC CAGTAGCGA	780
	809

(2) INFORMATION FOR SEQ ID NO: 119:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Abiotrophia defectiva*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

CGGCGCGATC CTCGTTGTAT CTGCTGCTGA CGGCCCAATG CCACAAACTC	60
GTGAACACAT CCTCTTGTCT CGTCAAGTTG GTGTTCTTA CATCGTAGTA TTCTTGAACA	120

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GGTTGACGAC GAAGAATTGC TCGAATTAGT TGAAATGGAA GTTCGTGACC TCTTGTCTGA	180
ATACGACTTC CCAGGCGACG ACACTCCAGT TATCGCTGGT TCAGCTTGAA AAGCTTTAGA	240
AGGCGACGCT AACTACGAAG CTAAAGTTT AGAATTGATG GAACAAGTTG ATGCTTACAT	300
TCCAGAACCA GAACGTGACA CTGACAAGCC ATTCAATGATG CCAGTCGAAG ACGTATTCTC	360
TATCACTGGT CGTGGTACTG TTGCAACTGG TCAGTGGTAA CGTGGTCAAG TTTCGCGTTGG	420
TGACGAAGTT GAAATCGTTG GTATCGAAGA AGAAACTTCT AAGACTACCG TTACCGGTGT	480
TGAAATGTT CGTAAGTTAT TGGATTACGC TGAAGCTGGG GACAACGTTG GTACCTTGTT	540
ACGTGGTGTAACTCGTACCCAAATCCAACG TGGTCAAGTA TTATCTAAAC CAGGTTCAAT	600
CACTCCGYAC ACTAAGTTCG AAGCTGAAGT GTACGTATTG TCTAAAGAAG AAGGTGGTCG	660
TCACACTCCA TTCTTCTCTA ACTACCGTCC ACAATTCTAC TTCCGTACAA CTGACGTAAC	720
TGGTGGTGTAACTTACAG AAGGTACTGA AATGGTTATG CCAGGCGACA ACGTACAAAT	780
GGTTGTTGAA TTGATCCACC CAATCGCGAT CGAAGAA	817

## (2) INFORMATION FOR SEQ ID NO: 120:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 754 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Candida albicans*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

CTCTGTCAAA TGGGACAAAA ACAGATTGA AGAAATCATC AAGGAAACCT CCAACTTCGT	60
CAAGAAGGTT GGTTACAACC CAAAGACTGT TCCATTGTT CCAATCTCTG GTTGAATGG	120
TGACAACWTG ATTGAASCAT CCACCAACTG TCCATGGTAC AAGGGTTGGG AAAAGGAAAC	180
CAAATCCGGT AAAGTTACTG GTAAGACCTT GTTACAAGCT ATTGACGCTA TTGAACCACC	240
AACCAGACCA ACCGACAAAC CATTGAGATT GCCATTRCAA GATGTTACAGATCGGTGG	300
TATTGGTACT GTGCCAGTCG GTAGAGTTGA AACTGGTATC ATCAAAGCCG GTATGGTWGT	360
TACTTTCGCC CCAGCTGGTG TTACCACTGA AGTCAARTCC GTTGAATGC ATCACGAACA	420
ATTGGCTGAA GGTGGTCCAG GTGACAATGT TRGTTCAAC GTTAAGAACR TTTCCGTTAA	480
AGAAATTAGA AGAGGTAACG TTTGTGGTGA CTCCAAGAAC GATCCACCAA AGGGTTGTGA	540

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CTCTTTCAAT GCCCAAGTCA TTGTTTGAA CCATCCAGGT CAAATCTCTG CTGGTTACTC	600
TCCAGTCTTG GATTGTCACR CTGCCACAT TGCTTGTAAA TTCGACRCTT TGGTTGAAAA	660
GATTGACAGA AGAACTGGTA AGRAATTGGA AGAAAATCCA AAATTCGTCA AATCCGGTGA	720
TGCTGCTATC GTCAAGATGG TCCCAACCAA ACCA	754

(2) INFORMATION FOR SEQ ID NO: 121:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 753 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Candida glabrata*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

TCTGTCAAGT GGGATGAATC CAGATTGCT GAAATCGTTA AGGAAACCTC CAACTTCATC	60
AAGAAGGTCG GTTACAACCC AAAGACTGTT CCATTGTCG CAATCTCTGG TTGGAACGGT	120
GACAACATGA TTGAAGCCAC CACCAACGCT TCCTGGTACA AGGGTTGGGA AAAGGAAACC	180
AAGGCTGGTG TCGTCAAGGG TAAGACCTTG TTGGAAGCCA TTGACGCTAT CGAACCCACCA	240
ACCAGACCAA CTGACAAGCC ATTGAGATTG CCATTGCAAG ATGTCTACAA GATCGGTGGT	300
ATCGGTACGG TGCCAGTCGG TAGAGTCGAA ACCGGTGTCA TCAAGCCAGG TATGGTTGTT	360
ACCTTCGCCCG CAGCTGGTGT TACCACTGAA GTCAAGTCCG TTGAAATGCA CCACGAACAA	420
TTGACTGAAG GTTTGCCAGG TGACAACGTT GGTTCAACG TTAAGAACGT TTCCGTTAAG	480
GAAATCAGAA GAGGTAATGT CTGTGGTGAC TCCAAGAACG ACCCACCAAA GGCTGCTGCT	540
TCTTTCAACG CTACCGTCAT TGTCTTGAAC CACCCAGGTC AAATCTCTGC TGGTTACTCT	600
CCAGTTTGG ACTGTACAC CGCCACATT GCTTGTAAAGT TCGAAGAATT GTTGGAAAAG	660
AACGACAGAA GATCCGGTAA GAAGTTGGAA GACTCTCAA AGTTCTTGAA GTCCGGTGAC	720
GCTGCTTGG TTAAGTTCGT TCCATCCAAG CCA	753

(2) INFORMATION FOR SEQ ID NO: 122:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 752 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Candida krusei*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

CCGTTAAGTG GGATGAAAAC AGATTTGAAG AAATTGTC	60
AA GGAAACCCAA AACTTCATCA	
AGAAGGTTGG TTACAACCCA AAGACTGTT	120
C CATTGTTCC AATCTCTGGT TGGAATGGT	
ACAACATGAT TGAAGCATCC ACCAACTGTC CATGGTACAA GGGTTGGACT AAGGAAACCA	180
AGGCAGGTGT TGTAAAGGGT AAGACCTTAT TAGAAGCAAT CGATGCTATT GAACCACCTG	240
TCAGACCAAC CGAAAAGCCA TTAAGATTAC CATTACAAGA TGTTTACAAG ATTGGTGGTA	300
TTGGTACTGT GCCAGTCGGT AGAGTCGAAA CCGGTGTCAT TAAGCCAGGT ATGGTTGTCA	360
CTTTGCTCC AGCAGGTGTC ACCACCGAAG TCAAATCCGT TGAAATGCAC CATGAACAAT	420
TAGAACAAAGG TGTTCCAGGT GATAACGTTG GTTCAACGT TAAGAACGTY TCTGTCAAGG	480
ATATCAAGAG AGGTAACGTT TGTGGTGA	540
ACT CCAAGCA CCCACCAATG GGTGCAGCTT	
CTTTCAATGC TCAAGTCATT GTCTTGAACC ACCCTGGTCA AATTTCGCT GGTTACTCTC	600
CAGTCTTGGG TTGTCACACT GCCCACATTG CATGTAAGTT CGACGAATTA ATCGAAAAGA	660
TTGACAGAAG AACTGGTAAG TCTGTTGAAG ACCATCCAAA GTCYGTCAAG TCTGGTGATG	720
CAGCTATCGT CAAGATGGTC CCAACCAAGC CA	752

(2) INFORMATION FOR SEQ ID NO: 123:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 754 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Candida parapsilosis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

CTCAGTCAAA TGGGACAAGA RCAGATACGA AGAAATTGTC AAGGAAACTT CCAACTTCGT	60
CAAGAAGGTT GGTTACAACC C TAAAGCTGT CCCATTGTC CCAATCTCTG GTTGGAACGG	120
TGACAATATG ATTGAACCAT CAACCAACTG TCCATGGTAC AAGGGTTGGG AAAAGGAAAC	180
TAAAGCTGGT AAGGTTACCG GTAAGACCTT GTTGGAAAGCT ATCGATGCTA TCGARCCACC	240

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AACCAGACCA	ACTGACAAGC	CATTGAGATT	GCCATTGCAA	GATGTCTACA	AGATTGGTGG	300
TATTGGAACT	GTGCCAGTTG	GTAGAGTTGA	AACCGGTATC	ATCAAGGCTG	GTATGGTTGT	360
TACCTTGC	CCAGCTGGTG	TTACCACTGA	AGTCAAGTCC	GTTGAAATGC	ACCACGAACA	420
ATTGACTGAA	GGTGTCCCAG	GTGACAATGT	TGGTTCAAC	GTCAAGAACG	TTTCAGTTAA	480
GGAAATCAGA	AGAGGTAACG	TYTGTGGTGA	CTCCAAGAAC	GATCCACCAA	AGGGATGTGA	540
YTCCTTCAAT	GCTCAAGTTA	TTGTCTTGAA	CCACCCAGGT	CAAATCTCTG	CTGGTTACTC	600
ACCAGTCTTG	GATTGTCACA	CTGCCACAT	TGCTTGTAAA	TTCGACACTT	TGATTGAAAA	660
GATTGACAGA	AGAACCGGTA	AGAAATTGGA	AGWTGAACCA	AAATTCACTCA	AGTCCGGTGA	720
TGCTGCYATC	GTCAAGATGG	TCCCAACCAA	GCCA			754

(2) INFORMATION FOR SEQ ID NO: 124:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 753 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Candida tropicalis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

TCTGTTAAAT	GGGACAARAA	CAGATTGAA	GAAATTATCA	AGGAAACYTC	TAACCTCGTC	60
AAGAAGGTTG	GTTACAACCC	TAAGGCTGTT	CCATTCTGTC	CAATCTCWGG	TTGGAATGGT	120
GACAACATGA	TTGAAGCTTC	TACCAACTGT	CCATGGTACA	AGGGTTGGGA	AAAAGAAACC	180
AAGGCTGGTA	AGGTTACCGG	TAAGACTTTG	TTGGAAGCCA	TTGATGCTAT	TGAACCACCT	240
TCAAGACCAA	CTGACAAGCC	ATTGAGATTG	CCATTGCAAG	ATGTTACAA	GATTGGTGGT	300
ATTGGTACTG	TGCCAGTCGG	TAGAGTTGAA	ACTGGTGTCA	TCAAAGCCGG	TATGGTTGTT	360
ACTTTYGCCC	CAGCTGGTGT	TACCACTGAA	GTCAAATCCG	TYGAAATGCA	CCACGAACAA	420
TTGGCTGAAG	GTGTCCCAGG	TGACAATGTT	GGTTCAACG	TTAAGAACGT	TTCTGTTAAA	480
GAAATTAGAA	GAGGTAACGT	TTGTGGTGAC	TCCAAGAACG	ATCCACCAA	GGGTTGTGAC	540
TCTTCAACG	CTCAAGTTAT	TGTCTTGAAAC	CACCCAGGTC	AAATYTCTGC	TGGTTACTCT	600
CCAGTCTTGG	ATTGTCACAC	TGCTCATATT	GCTTGAAAT	TCGACACCTT	GGTTGAAAAG	660
ATTGACAGAA	GAACTGGTAA	GAAATTGGAA	GAAAATCCAA	AATTGTCAA	ATCCGGTGAT	720

GCTGCTATTG TCAAGATGGT TCCAACCAAA CCA

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## (2) INFORMATION FOR SEQ ID NO: 125:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Corynebacterium accolens*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

CGCGGCTATC CTGGTTGTTG CTGCAACCGA TGGCCCGATG CCGCAGACCC GCGAGCACGT	60
TCTGCTTGCT CGCCAGGTTG GCGTTCTTA CATCCTCGTT GCACTGAACA AGTGCACAT	120
GGTTGATGAT GAGGAAATCA TCGAGCTCGT GGAGATGGAG ATCTCCGAGC TGCTCGCAGA	180
GCAGGACTAC GATGAGGAAG CTCCTATCGT TCACATCTCC GCTCTGAAGG CACTCGAGGG	240
TGACGAGAAG TGGGTACAGT CCATCGTTGA CCTGATGGAT GCCTGCGACA ACTCCATCCC	300
TGATCCGGAG CGCGCTACCG ATCAGCCGTT CTTGATGCCT ATCGAGGACA TCTTCACCAT	360
TACCGGCCGC GGTACCGTTG TTACCGGCCG TGTTGAGCGT GGTCGTCTGA ACGTCAACGA	420
GGACGTTGAG ATCATCGGT A TCCAGGAGAA GTCCCAGAAC ACCACCGTTA CCGGTATCGA	480
GATGTTCCGC AAGATGATGG ACTACACCGA GGCTGGCGAC AACTGTGGTC TGCTTCTGCG	540
TGGTACCAAG CGTGAGGACG TTGAGCGTGG CCAGGTTGTT ATCAAGCCGG GCGCTTACAC	600
CCCTCACACC AAGTCGAGG GTTCCGTCTA CGTCCTGAAG AAGGAAGAGG GCGGCCGCCA	660
CACCCCGYTC ATGAACAACT ACCGTCTCA GTTCTACTTC CGCACCAACCG ACGTTACCGG	720
TGTTGTGAAC CTGCCTGAGG GCACCGAGAT GGTTATGCCT GGCGACAACG TTGAGATGTC	780
TGTTGAGCTC ATCCAGCCTG TTGCTATGGA CGAG	814

## (2) INFORMATION FOR SEQ ID NO: 126:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Corynebacterium diphtheriae*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

CGCGCAATC CTCGTTGTTG CTGCCACCGA CGGCCAATG CCTCAGACCC GTGAGCACGT	60
TCTGCTCGCT CGCCAGGTCG GCGTTCTTA CATCCTCGTT GCTCTGAACA AGTGCACAT	120
GGTTGATGAT GAGGAAATCA TCGAGCTCGT CGAGATGGAG ATCCRTGAGC TGCTCGCTGA	180
GCAGGATTAC GACGAAGAGG CTCCAATCAT CCACATCTCC GCACTGAAGG CTCTTGAGGG	240
CGACGAGAAG TGGACCCAGT CCATCATCGA CCTCATGCAG GCTTGCKATG ATTCCATCCC	300
AGACCCAGAG CGTGAGACCG ACAAGCCATT CCTCATGCCT ATCGAGGACA TCTTCACCAT	360
CACCGGCCGC GGTACCGTTG TTACCGGCCG TGTTGAGCGT GGCTCCCTGA AGGTCAACGA	420
GGACGTCGAG ATCATCGTA TCCGCGAGAA KGCTACCACC ACCACCGTTA CCGGTATCGA	480
GATGTTCCGT AAGCTTCTCG ACTACACCGA GGCTGGCGAC AACTGTGGTC TGCTTCTCCG	540
TGGCGTTAAG CGCGAAGACG TTGAGCGTGG CCAGGTTGTT GTTAAGCCAG GCGCTTACAC	600
CCCTCACACC GAGTCGAGG GCTCTGTCTA CGTTCTGTCC AAGGACGAGG GTGGCCGCCA	660
CACCCCATTC TTCGACAAC ACCGCCACA GTTCTACTTC CGCACCACCG ACGTTACCGG	720
TGTTGTGAAG CTTCTGAGG GCACCGAGAT GGTCTATGCCT GGCGACAACG TCGACATGTC	780
CGTCACCCCTG ATCCAGCCTG TCGCTATGGA TGAG	814

## (2) INFORMATION FOR SEQ ID NO: 127:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Corynebacterium genitalium*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

CGCGCCATC CTGGTTGTTG CTGCAACCGA TGGCCCGATG CCGCAGACCC GTGAGCACGT	60
TCTGCTGGCT CGCCAGGTTG GCGTTCCGTA CATCCTAGTT GCACTGAACA AGTGCACAT	120
GGTTGATGAT GAGGAGCTGC TGGAGCTCGT CGAGATGGAG GTCCCGCGAGC TGCTGGCTGA	180
GCAGGACTTC GACGAGGAAG CACCTGTTGT TCACATCTCC GCACTGAAGG CCCTGGAGGG	240
CGACGAGAAG TGGGCTAAGC AGATCCTGGA GCTCATGGAG GCTTGCGACA ACTCCATCCC	300

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GGATCCGGAG CGCGAGACCG ACAAGCCGTT CCTGATGCCG GTTGRGGACA TCTTCACCAT	360
TACCGGCCGC GGTACCGTTG TTACCGGCCG TGTTGAGCGT GGCGTCTGA ACCTGAACGA	420
CGAGGTCGAG ATCCTGGCA TCCGCGAGAA GTCCACCAAG ACCACCGTTA CCTCCATCGA	480
GATGTTAAC AAGCTGCTGG ACACCGCAGA GGCTGGCGAC AACGCCGCAC TGCTGCTGCG	540
TGGCCTGAAG CGCGAAGATG TTGAGCGTGG TCAGATCGTT GCTAAGCCGG GCGAGTACAC	600
CCCGCACACC GAGTCGAGG GCTCCGTCTA CGTTCTGTCC AAGGACGAGG GTGGCCGCCA	660
CACCCCGTTC TTCGACAACT ACCGTCCGCA GTTCTATTTC CGCACCACCG ACGTTACCGG	720
TGTTGTGAAG CTGCCGGAGG GCACCGAGAT GGTTATGCCG GGCGACAACG TTGACATGTC	780
CGTCACCCTG ATCCAGCCGG TTGCTATGGA CGAG	814

(2) INFORMATION FOR SEQ ID NO: 128:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Corynebacterium jeikeium*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

CGCGCCATC CTGGTTGTTG CCGCAACCGA TGGCCCGATG CCGCAGACCC GCGAGCACGT	60
TCTGCTGGCY CGCCAGGTTG GCGTTCCGTA CATCCTGGTT GCACTGAACA AGTGTGACAT	120
GGTTGACGAT GAGGAGCTGC TGGAGCTCGT CGAGATGGAG GTCCGCGAGC TGCTGGCTGA	180
GCAGGACTTC GACGAGGAAG CTCCGGTTGT TCACATCTCC GCACTGAAGG CCCTGGAGGG	240
CGACGAGAAG TGGGCTAACCC AGATTCTCGA GCTGATGCAG GCTTGCACG AGTCTATCCC	300
GGATCCGGAG CGCGAGACCG ACAAGCCGTT CCTGATGCCG GTTGWGGACA TCTTCACCAT	360
TACCGGTGCG GGTACCGTTG TTACCGGCCG TGTTGAGCGT GGCGATCCTGA ACCTGAACGA	420
CGAGGTTGAG ATCCTGGTA TCCGCGAGAA GTCCCGAGAAG ACCACCGTTA CCTCCATCGA	480
GATGTTAAC AAGCTGCTGG ACACCGCAGA GGCTGGCRAC AACGCTGCAC TGCTGCTGCG	540
TGGTCTGAAG CGCGAGGACG TTGAGCGTGG CCAGATCATC GCTAAGCCGG GCGAGTACAC	600
CCCGCACACC GAGTCGAGG GCTCCGTCTA CGTTCTGTCC AAGGACGAGG GTGGCCGCCA	660
CACCCCGTTC TTCGACAACT ACCGTCCGCA GTTCTACTTC CGCACCACCG ACGTTACCGG	720

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TGTTGTGAAG CTGCCTGAGG GCACCGAGAT GGTTATGCCG GGCGACAACG TYGACATGTC 780

CGTCACCCCTG ATCCAGCCGG TTGCTATGGA CGAG 814

## (2) INFORMATION FOR SEQ ID NO: 129:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 748 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Corynebacterium pseudodiphtheriticum*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:

CGGCGCTATC TTGGTTGTTG CAGCTACCGA CGGCCCAATG CCACAGACTC GCGAGCACGT 60

TCTGCTGGCT CGCCAGGTTG GCGTTCCCTA CATCTGGTT GCACTAAACA AGTGCACAT 120

GGTTGACGAC GAGGAAATCC TCGAGCTCGT CGAGATGGAG ATCCGCGAAT TGCTGGCTGA 180

CCAGGAATTG GACGAAGAAG CTCCAATCGT TCACATCTCC GCAGTCGGCG CCTTGGAAAGG 240

CGAAGAGAGG TGGGTTAACG CCATCGTTGA ACTGATGGAT GCTTGTGACG AGTCGATCCC 300

TGATCCAGAC CGTGCTACCG ACAAGCCATT CCTGATGCCT ATCGAGGACA TCTTCACCAT 360

TACCGGTCGT GGCACCGTTG TTACGGGTCG TGTTGAGCGT GGTTCCCTGA AGGTCAACGA 420

AGAAGTCGAG ATCATCGGCA TCAAGGAAA GTCCCAGAAG ACCACCATCA CCGGTATCGA 480

AATGTTCCGC AAGATGCTGG ACTACACCGA GGCCGGCGAC AACGCTGGTC TGCTGCTTCG 540

CGGTACCAAG CGTGAAGACG TTGAGCGTGG ACAGGTTATC GTTGCTCCAG GTGCTTACAG 600

CACCCACAAG AAGTCGAAG GTTCCGTCTA CGTTCTTCC AAGGACGAGG GCGGCCGCCA 660

CACCCCGTTC TTGACAACT ACCGTCCCTA GTTCTACTTC CGCACCACCG ACGTTACCGG 720

TGTTGTTACC CTGCCTGAGG GCACCGAG 748

## (2) INFORMATION FOR SEQ ID NO: 130:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 813 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Corynebacterium striatum*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:

GGCGCTATCT	TGGTTGTTGC	TGCAACCGAT	GGCCCGRTGC	CGCAGACCCG	CGAGCACGTT	60
CTTCTGGCTC	GCCAGGTTGG	CGTTCCCTAC	ATCCTCGTTG	CACTGAACAA	GTGCGACATG	120
GTTGACGACG	AGGAAATTAT	CGAGCTCGTC	GAGATGGAGA	TCCGCGAACT	GCTCGCAGAG	180
CAGGACTACG	ATGAGGAAGC	TCCGATCGTT	CACATCTCTG	CTCTGAAGGC	TCTTGAGGGC	240
GRCGAGAAAGT	GGGTACAGGC	TATCGTTGAC	CTGATGCAGG	CTTGCATGATGA	CTCCATCCCG	300
GATCCGGAGC	GCGAGCTGGA	CAAGCCGTT	CTGATGCCAA	TCGAGGACAT	CTTCACCACATC	360
ACCGGCCGCG	GTACCGTTGT	TACTGGCCGT	GTTGAGCGTG	GCTCCCTGAA	CGTCAACGAG	420
GACGTTGAGA	TCATCGGTAT	CCAGGACARG	TCCATCTCCA	CCACCGTTAC	CGGTATCGAG	480
ATGYTCCGCA	AGATGATGGA	CTACACCGAG	GCTGGCGACA	ACTGTGGTCT	GCTTCTGCGT	540
GGTACCAAGC	GTGAAGAGGT	TGAGCGCGGC	CAGGTTGTTA	TTAAGCCGGG	CGCTTACACC	600
CCTCACACCC	AGTTCGAGGG	TTCCGTCTAC	GTCCTGAAGA	AGGAAGAGGG	CGGCCGCCAC	660
ACCCCGTTCA	TGGACAACTA	CCGTCCGCAG	TTCTACTTCC	GCACCACCGA	CGTTACCGGC	720
GTCATCAAGC	TGCCTGAGGG	CACCGAGATG	GTTATGCCTG	GCGACAACGT	CGAGATGTCTY	780
GTCGAGCTGA	TCCAGCCGGT	CGCTATGGAC	GAG			813

## (2) INFORMATION FOR SEQ ID NO: 131:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Enterococcus avium*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

CGGAGCTATC	TTAGTAGTAT	CTGCTGCTGA	TGGCCCTATG	CCTCAAACTC	GTGAACACAT	60
CTTGTATCT	CGTAACGTTG	GTGTTCTTA	CATCGTTGTA	TTCTTAAACA	AAATGGATAT	120
GGTTGACGAT	GAAGAATTAC	TTGAATTAGT	TGAAATGGAA	GTTCGTGACT	TATTAACGTGA	180
ATACGACTTC	CCAGGCGACG	ACACTCCAGT	TATCGCAGGT	TCAGCGTTGA	AAGCTTTAGA	240
AGGCGACGCT	TCATACGAAG	AAAAAATCTT	AGAATTAATG	GCTGCTGTTG	ACGAATATAT	300

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CCCAACACCA GTTCGTGATA CTGACAAACC ATTCACTGATG CCAGTCGAAG ACGTATTCTC	360
AATCACTGGT CGTGGTACTG TTGCAACTGG TCGTGTGAA CGTGGACAAG TTCGCGTTGG	420
TGACGAAGTT GAAATCGTAG GTATCGCTGA CGAAACTGCT AAAACAACGT TTACAGGTGT	480
TGAAATGTT CGTAAATTGT TAGACTACGC TGAAGCAGGT GACAACATCG GTGCTTGTT	540
ACGTGGTGT GCACGTGAAG ATATCCAACG TGGACAAGTA TTGGCTAAC CAGCTTCAAT	600
CACTCCACAT ACAAAATTCT CTGCAGAAGT TTATGTTCTA ACTAAAGAAG AAGGTGGACG	660
TCATACTCCA TTCTTCACTA ACTACCGTCC TCAGTTCTAC TTCCGTACAA CTGACGTAAC	720
TGGTAGTT GATCTACCAAG AAGGTACTGA AATGGTWATG CCTGGGGATA ACGTAACATAT	780
GGAAGTTGAA TTGATYCACC CAATYGCAGT AGAAGAC	817

(2) INFORMATION FOR SEQ ID NO: 132:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Enterococcus faecalis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

CGGAGCTATC TTAGTAGTTT CTGCTGCTGA TGGTCCTATG CCTCAAACAC GTGAACATAT	60
CTTATTATCA CGTAACGTTG GTGTACCATATA CATCGTTGTA TTCTTAAACA AAATGGATAT	120
GGTTGATGAC GAAGAATTAT TAGAATTAGT AGAAATGGAA GTTCGTGACT TATTATCAGA	180
ATACGATTTCC CCAAGCGATG ATGTTCCAGT TATCGCAGGT TCTGCTTGA AAGCTTTAGA	240
AGGCGACGAG TCTTATGAAG AAAAATCTT AGAATTAATG GCTGCAGTTG ACGAATATAT	300
CCCAACTCCA GAACGTGATA CTGACAAACC ATTCACTGATG CCAGTCGAAG ACGTATTCTC	360
AATCACTGGA CGTGGTACTG TTGCTACAGG ACGTGTGAA CGTGGTGAAG TTCGCGTTGG	420
TGACGAAGTT GAAATCGTTG GTATTAAAGA CGAAACATCT AAAACAACYG TTACAGGTGT	480
TGAAATGTT CGTAAATTAT TAGACTACGC TGAAGCAGGC GACAACMTCG GTGCTTTATT	540
ACGTGGTGT GCACGTGAAG ATATCGAACG TGGACAAGTA TTAGCTAAC CAGCTACAAT	600
CACTCCACAC ACAAAATTCA AAGCTGAAGT ATACGTATTA TCAAAAGAAG AAGGCAGGACG	660
TCACACTCCA TTCTTCACTA ACTACCGTCC TCAATTCTAC TTCCGTACAA CAGACGTTAC	720

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TGGTGTGTA GAATTGCCAG AAGGTACTGA AATGGTAATG CCTGGTGATA ACGTTGCTAT	780
GGACGTTGAA TTAATTCACC CAATCGCTAT CGAAGAC	817

(2) INFORMATION FOR SEQ ID NO: 133:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 774 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Enterococcus faecium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

CGGAGCTATC TTGGTAGTTT CTGCTGCTGA CGGCCAATG CCTCAAACATC GTAACACAT	60
CCTATTGTCT CGTCAAGTTG GTGTTCTTA CATCGTTGTA TTCTTGAACA AAGTAGACAT	120
GGTTGATGAC GAAGAATTAC TAGAATTAGT TGAAATGGAA GTTCGTGACC TATTAACAGA	180
ATACRAATTCT CCTGGTGRCG ATGTTCTGT AGTTGCTGGA TCAGCTTGA AAGCTCTAGA	240
AGGCACGCT TCATACGAAG AAAAAATTCT TGAATTATG GCTGCAGTTG ACGAATACAT	300
CCCAACTCCA GAACGTGACA ACGACAAACC ATTCATGATG CCAGTTGAAG ACGTGTCTC	360
AATTACTGGA CGTGGTACTG TTGCTACAGG TCGTGGTGAAG CGTGGACAAG TTTCGCGTTGG	420
TGACGAAGTT GAAGTTGTTG GTATTGCTGA AGAAACTTCA AAAACAACAG TTACTGGTGT	480
TGAAATGTT CGTAAATTGT TAGACYACGC TGAAGCTGGA GACRACATTG GTGCTTTACT	540
ACGTGGTGT GCACGTGAAG ACATCCAACG TGGACAAGTT TTAGCTAAC CAGGTACAAT	600
CACACCTCRT AAAAAATTCT CTGCAGAAAGT ATACGTGTTG AAAAAAGAAG AAGGTGGACG	660
TCATACTCCA TTCTTCACTA ACTACCGTCC ACAATTCTAC TTCCGTACAA CTGACGTAAC	720
AGGTGTTGTT GAATTACCAAG AAGGAACGTGA AATGGTCATG CCCGGTGACA ACGT	774

(2) INFORMATION FOR SEQ ID NO: 134:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 809 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Enterococcus gallinarum*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

CGGTGCGATC TTAGTAGTAT CTGCTGCTGA CGGTCCATG CCTCAAACAT	60
CTTGTATCA CGTAACGTTG GCGTACCAT AATCGTTGTT TTCTTGAACA AAATGGATAT	120
GGTTGAYGAC GAAGAATTGC TAGAATTAGT TGAAATGGAA GTTCGTGACC TATTGTCTGA	180
ATATGACTTC CCAGGCGACG ATGTTCTGT AATGCCGGT TCTGCTTGA AAGCTCTGA	240
AGGAGATCCT TCATACGAAG AAAAAATCAT GGAATTGATG GCTGCAGTTG ACGAATACGT	300
TCCAACCTCCA GAACGTGATA CTGACAAACC ATTCATGATG CCAGTCGAAG ACGTATTCTC	360
AATCACTGGA CGTGGTACTG TTGCTACAGG CCGTGTGAA CGTGGACAAG TTCGCGTTGG	420
TGATGAAGTA GAAATCGTTG GTATTGCTGA CGAAACTGCT AAAACAAC TG TAACAGGTGT	480
TGAAATGTTG CGTAAATTGT TAGACTATGC TGAAGCAGGG GATAACATTG GTGCATTGCT	540
ACGTGGGGTT GCTCGTGAAG ACATCCAACG TGGACAAGTA TTGGCTAAAG CTGGTACAAT	600
CACACCTCAT ACAAAATTCA AAGCTGAAGT TTATGTTTG ACAAAAGAAG AAGGTGGACG	660
TCACACCTCCA TTCTTCACTA ACTACCGTCC TCAGTTCTAC TTCCGTACAA CTGACGTAAC	720
TGGTGTGTT GAATTACCAAG AAGGAACGTGA AATGGTGATG CCTGGCGACA ACGTGACCAT	780
CGACGTTGAA TTGATRCACC CAATCGCTC	809

## (2) INFORMATION FOR SEQ ID NO: 135:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 823 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Gardnerella vaginalis*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

TGGCGCAATC CTCGTGGTTG CTGCTACCGA CGGTCCAATG GCTCAGACCC GTGAACACGT	60
CTTGCTTGCT AAGCAGGTGCG GCGTTCCAAA AATTCTTGTGTT GCTTTGAACA AGTGCAGATAT	120
GGTTGACGAC GAAGAGCTTA TCGATCTCGT TGAAGAAGAG GTCCGTGACC TCCTCGAAGA	180
AAACGGCTTC GATCGCGATT GCCCAGTCYT CCGTACTTCC GCTTACGGCG CTTTGCATGA	240
TGACGCTCCA GACCACGACA AGTGGGTAGA GACCGTCAAG GAACTCATGA AGGCTGTTGA	300

CGAGTACATC CCAACCCAA CTCACGATCT TGACAAGCCA TTCTTGATGC CAATCGAAGA	360
TGTGTTCAACC ATCTCCGGTC GTGGTYCCGT TGTCACCGGT CGTGTGAGC GTGGTAAGCT	420
CCCAATCAAC ACCCCAGTTG AGATCGTTGG TTTGCGCGAT ACCCAGACCA CCACCGTCAC	480
CTCTATCGAG ACCTTCCACA AGCAGATGGA TGAGGCAGAG GCTGGCGATA ACACTGGTCT	540
TCTTCTCCGC GGTATCAACC GTACCGACGT TGAGCGTGGT CAGGTTGTGG CTGCTCCAGG	600
TTCTGTGACT CCACACACCA AGTCGAAGG CGAAGTTAC GTCTTGACCA AGGACGAAGG	660
TGGCCGTCAC TCGCCATTCT TCTCCAACTA CCGTCCACAG TTCTACTTCC GTACCACCGA	720
TGTTACTGGC GTTATCACCT TGCCAGACGG CATCGAAATG GTTCAGCCAG GCGATCACGC	780
AACCTTCACT GTTGAGTTGA TCCAGGCTAT CGCAATGGAA GAG	823

## (2) INFORMATION FOR SEQ ID NO: 136:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Listeria innocua*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:

CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAAACTC GTGAACATAT	60
CTTACTTTCA CGTCAAGTTG GTGTTCCATA CATCGTTGTA TTCATGAACA AATGTGACAT	120
GGTTGACGAT GAAGAATTAC TAGAATTAGT TGAAATGGAA ATTCTGTGATC TATTAACTGA	180
ATATGAATTTC CCTGGCGATG ACATTCTGT AATCAAAGGT TCAGCTCTTA AAGCACTTCA	240
AGGTGAAGCT GACTGGGAAG CTAAAATTGA CGAGTTAATG GAAGCTGTAG ATTCTTACAT	300
TCCAACCTCCA GAACGTGATA CTGACAAACC ATTCTATGATG CCAGTTGAGG ATGTATTCTC	360
AATCACTGGT CGTGGAACAG TTGCAACTGG ACGTGTGAA CGTGGACAAG TTAAAGTTGG	420
TGACGAAGTA GAAGTTATCG GTATTGAAGA AGAAAGCAAA AAAGTAGTAG TAACTGGAGT	480
AGAAATGTTC CGTAAATTAC TAGACTACGC TGAAGCTGGC GACAACATTG GCGCACTTCT	540
ACGTGGTGTGTT GCTCGTGAAG ATATCCAACG TGGTCAAGTA TTAGCTAAC CAGGTTCGAT	600
TACTCCACAC ACTAACTTCA AAGCTGAAAC TTATGTTTTA ACTAAAGAAG AAGGTGGACG	660
TCACACTCCA TTCTTCAACA ACTACCGCCC ACAATTCTAT TTCCGTACTA CTGACGTAAC	720

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TGGTATTGTT ACACCTCCAG AAGGTACTGA AATGGTAATG CCTGGTGATA ACATTGAGCT 780

TGCAGTTGAA CTAATTGCAC CAATCGCTAT CGAAGAC 817

## (2) INFORMATION FOR SEQ ID NO: 137:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 818 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Listeria ivanovii*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGTCCAATG CCACAAACTC GTGAACATAT 60

TCTTACTTTC ACGTCAAGTT GGTGTTCCAT ACATCGTTGT ATTCACTGAAAC AAATGTGACA 120

TGGTTGACGA TGAAGAATTAA CTTGAATTAG TTGAAATGGA AATTCTGTGAT CTATTAAC TG 180

AATATGAATT CCCTGGCGAC GACATTCCCTG TAATCAAAGG TTCAGCTCTT AAAGCACTTC 240

AAGGTGAAGC TGATTGGAA GCTAAAATTG ACGAGTTAAT GGAAGCTGTA GATTCTTACA 300

TTCCAACCTCC AGAACGTGAT ACTGACAAAC CATTCACTGAT GCCAGTTGAG GATGTATTCT 360

CAATCACTGG TCGTGGAAACA GTTGCAACTG GACGTGTTGA ACGTGGACAA GTTAAAGTTG 420

GTGACGAAGT AGAAGTTATC GGTATTGAAG AAGAAAGCAA AAAAGTAGTA GTAACTGGAG 480

TAGAAATGTT CCGTAAATTAA CTAGACTACG CTGAAGCTGG CGACAACATT GGCGCACTTC 540

TACGTGGTGT TGCTCGTGAA GATATCCAAC GTGGTCAAGT ATTAGCTAAA CCAGGTTCGA 600

TTACTCCACA TACTAACTTC AAAGCTGAAA CTTATGTTTT AACTAAAGAA GAAGGTGGAC 660

GTCATACTCC ATTCTTCAAC AACTACCGCC CACAATTCTA TTTCCGTACT ACTGACGTAA 720

CTGGTATTGT TACACTTCCA GAAGGTACTG AAATGTAAT GCCTGGTGAT AACATTGAGC 780

TTGCAGTTGA ACTAATTGCA CCAATCGCTA TCGAAGAC 818

## (2) INFORMATION FOR SEQ ID NO: 138:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

(A) ORGANISM: *Listeria monocytogenes*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAAACTC GTGAACATAT	60
CTTACTTTCA CGTCAAGTTG GTGTTCCATA CATCGTTGTA TTCATGAACA AATGTGACAT	120
GGTTGACGAT GAAGAATTAC TAGAATTAGT TGAAATGGAA ATTCTGTGATC TATTAACTGA	180
ATATGAATTC CCTGGCGATG ACATTCTGT AATCAAAGGT TCAGCTCTTA AAGCACTTCA	240
AGGTGAAGCT GACTGGGAAG CTAAAATTGA CGAGTTAATG GAAGCTGTAG ATTCTTACAT	300
TCCAACCTCCW GAACGTGATA CTGACAAACC ATTCACTGATG CCAGTTGAGG ATGTATTCTC	360
AATCACTGGT CGTGGAACAG TTGCAACTGG ACGTGTGAA CGTGGACAAG TTAAAGTTGG	420
TGACGAAGTA GAAGTTATCG GTATCGAAGA AGAAAGCAAA AAAGTAGTAG TAACTGGAGT	480
AGAAATGTTG CGTAAATTAC TAGACTACGC TGAAGCTGGC GACAACATTG GCGCACTTCT	540
ACGTGGTGTGTT GCTCGTGAAG ATATCCAACR TGGTCAAGTA TTAGCTAAC CAGGTTCGAT	600
TACTCCACAC ACTAACTTCA AAGCTGAAAC TTATGTTTTA ACTAAAGAAG AAGGTGGACG	660
TCACACTCCA TTCTTCAACA ACTACCGCCC ACAATTCTAT TTCCGTACTA CTGACGTAAC	720
TGGTATTGTT ACACTTCCAG AAGGTACTGA AATGGTAAYG CCTGGTGATA ACATTGAGCT	780
TGCAGTTGAA CTAATTGCAC CAATCGCTAT CGAAGAC	817

## (2) INFORMATION FOR SEQ ID NO: 139:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

(A) ORGANISM: *Listeria seeligeri*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAAACTC GTGAACATAT	60
CTTACTTTCA CGTCAAGTTG GTGTTCCATA CATCGTTGTA TTCATGAACA AATGTGACAT	120
GGTTGACGAT GAAGAATTAC TTGAATTAGT TGAAATGGAA ATTCTGTGATC TATTAACTGA	180
ATATGAATTC CCTGGTGATG ACATTCTGT AATCAAAGGT TCAGCTCTTA AAGCACTTCA	240

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AGGTGAAGCT GACTGGGAAG CTAAAATTGA CGAGTTAATG	300
TCCAACTCCA GAACGTGATA CTGACAAACC ATTCACTGATG	360
AATCACTGGT CGTGGAACTG TTGCAACTGG ACGTGTGAA CGTGGACAAG	420
TTAAAGTTGG TGACGAAGTA GAAGTTATCG GTATTGAAGA AGAAAGCAA	480
AAAGTAATAG TAACTGGAGT AGAAATGTT CGTAAATTAC TAGACTACGC	540
TGAAGCTGGC GACAACATTG GCGCACTTCT ACGTGGTGT GCTCGTGAAG ATATCCAACG	600
TGGTCAAGTA TTAGCTAAAC CAGGTTCGAT TACTCCACAT ACTAACTTCA AAGCTGAAAC	660
TTATGTTTTA ACTAAAGAAG AAGGTGGACG TCACACTCCA TTCTTCAACA ACTACCGCCC ACAATTCTAT	720
TTCCGTACTA CTGACGTAAC TGGTATTGTT ACACTTCCAG AAGGTACTGA AATGGTAATG CCTGGTGATA	780
ACATTGAGCT TGCAGTTGAA CTAATTGCAC CAATCGCTAT CGAAGAC	817

(2) INFORMATION FOR SEQ ID NO: 140:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Staphylococcus aureus*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

CGGTGGTATC TTAGTAGTAT CTGCTGCTGA CGGTCCAATG CCACAAACTC GTGAACACAT	60
TCTTTTATCA CGTAACGTTG GTGTACCAGC ATTAGTAGTA TTCTTAAACA AAGTTGACAT	120
GGTTGACGAT GAAGAATTAT TAGAATTAGT AGAAATGGAA GTTCGTACT TATTAAGCGA	180
ATATGACTTC CCAGGTGACG ATGTACCTGT AATCGCTGGT TCAGCATTAR AAGCTTTAGA	240
AGGCATGCT CAATACGAAG AAAAATCTT AGAATTARTG GAAGCTGTAG ATACTTACAT	300
TCCAACCTCCA GAACGTGATT CTGACAAACC ATTCACTGATG CCAGTTGAGG ACGTATTCTC	360
AATCACTGGT CGTGGTACTG TTGCTACAGG CCGTGTGAA CGTGGTCAA TCAAAGTTGG	420
TGAAGAAGTT GAAATCATCG GTTACATGA CACATCTAAA ACAACTGTTA CAGGTGTTGA	480
AATGTTCCGT AAATTATTAG ACTACGCTGA AGCTGGTGAC AACATTGGTG CATTATTACG	540
TGGTGTGCT CGTGAAGACG TACAACGTGG TCAAGTATTA GCTGCTCCTG GTTCAATTAC	600
ACCACATACT GAATTCAAAG CAGAAGTATA CGTATTATCA AAAGACGAAG GTGGACGTCA	660

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CACTCCATTC TTCTCAAACT ATCGTCCACA ATTCTATTTC CGTACTACTG ACGTAACACTG	720
TGTTGTTCAC TTACCAGAAG GTACTGAAAT GGTAATGCCT GGTGATAACG TTGAAATGAC	780
AGTAGAATTAA ATCGCTCCAA TCGCGATTGA AGAC	814

## (2) INFORMATION FOR SEQ ID NO: 141:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Staphylococcus epidermidis*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

CGGCGGTATC TTAGTTGTAT CTGCTGCTGA CGGTCCAATG CCACAAACTC GTGAACACAT	60
CTTATTATCA CGTAACGTTG GTGTACCAAGC ATTAGTTGTA TTCTTAAACA AAGTTGACAT	120
GGTAGACGAC GAAGAATTAT TAGAATTAGT TGAAATGGAA GTTCGTGACT TATTAAGCGA	180
ATATGACTTC CCAGGTGACG ATGTACCTGT AATCGCTGGT TCTGCATTAA AAGCATTAGA	240
AGGCGATGCT GAATACGAAC AAAAAATCTT AGACTTAATG CAAGCAGTTG ATGATTACAT	300
TCCAACCTCA GAACGTGATT CTGACAAACC ATTCAATGATG CCAGTTGAGG ACGTATTCTC	360
AATCACTGGT CGTGGTACTG TTGCTACAGG CCGTGGTCAA TCAAAGTWGG	420
TGAAGAAGTT GAAATCATCG GTATGCACGA AACTTCTAAA ACAACTGTTA CTGGTGTAGA	480
AATGTTCCGT AAATTATTAG ACTACGCTGA AGCTGGTGAC AACATCGGTG CTTTATTACG	540
TGGTGGTGC A CGTGAAGACG TACAACGTGG TCAAGTATTA GCTGCTCCTG GTTCTATTAC	600
ACCACACACA AAATTCAAAG CTGAAGTATA CGTATTATCT AAAGATGAAG GTGGACGTCA	660
CACTCCATTC TTCACAACT ATCGCCCACA ATTCTATTTC CRTACTACTG ACGTAACACTG	720
TGTTGTAAC TTACCAGAAG GTACAGAAAT GGTTATGCCT GGCGACAACG TTGAAATGAC	780
AGTTGAATTAA ATCGCTCCAA TCGCTATCGA AGAC	814

## (2) INFORMATION FOR SEQ ID NO: 142:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Staphylococcus saprophyticus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAAACTC GTGAACACAT	60
TCTTTTATCA CGTRACGTTG GTGYCCAGC ATTAGTTGTA TTCTTAAACA AAGTTGACAT	120
GGTTGACGAY GAAGAATTAT TAGAATTRGT AGAAATGGAA GTTCGTGRCT TATTAAGCGA	180
ATATGACTTC CCAGGTGACG ATGTACCTGT AATCTCTGGT TCTGCATTA AAGCTTTAGA	240
AGGCGACGCT GACTATGAGC AAAAAATCTT AGACTTAATG CAAGCTGTTG ATGACTYCAT	300
TCCAACACCA GAACGTGATT CTGACAAACC ATTCATGATG CCAGTTGAGG ACGTATTCTC	360
AATCACTGGT CGTGGTACTG TTGCTACAGG CCGTGTGAA CGTGGTCAAA TCAAAGTCGG	420
TGAAGAAAATC GARATCATCG GTATGCAAGA AGAATCAAGC AAAACAACGT TTACTGGTGT	480
AGAAATGTTC CGTAAATTAT TAGACTACGC TGAAGCTGGT GACAACATTG GTGCATTATT	540
ACGTGGTGTTC TCACGTGATG ATGTACAACG TGGTCAAGTT TTAGCTGCTC CTGGTACTAT	600
CACACCACAT ACAAAATTCA AAGCGGATGT TTACGTTTA TCTAAAGATG AAGGTGGTCG	660
TCATACGCCA TTCTTCACTA ACTACCGCCC ACAATTCTAT TTCCGTACTA CTGACGTAAC	720
TGGTGTGTT AACTTACCAAG AAGGTACTGA AATGGTTATG CCTGGCGATA ACGTTGAAAT	780
GGATGTTGAA TTAATTTCTC CAATCGCTAT TGAAGAC	817

(2) INFORMATION FOR SEQ ID NO: 143:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Staphylococcus simulans*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

CGGCGGGTATC TTAGTAGTAT CTGCTGCAGA TGGTCCAATG CCACAAACTC GTGAACACAT	60
CTTATTATCA CGTAACGTTG GTGTACCAAGC TTTAGTTGTA TTCTTAAACA AAGCTGACAT	120
GGTTGACGAC GAAGAATTAT TAGAATTAGT TGAAATGGAA GTTCGTGACT TATTATCTGA	180

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ATACGACTTC CCTGGTGACG ATGTACCACT TATCGTTGGT TCTGCATTAA AAGCTTTAGA	240
AGGCGACCCA GAATACGAAC AAAAAATCTT AGACTTAATG CAAGCTGTAG ATGACTACAT	300
CCCAACTCCA GAACGTGACT CTGATAAACCC ATTCACTGATG CCAGTTGAGG ACGTATTCTC	360
AATCACTGGT CGTGGTACTG TAGCAACAGG CCGTGGTCAA TCAAAGTCGG	420
TGAAGAAGTT GAAATCATCG GTATCACTGA AGAAAGCAAG AAAACAACAG TTACAGGTGT	480
AGAAATGTT CGTAAATTAT TAGACTACGC TGAAGCTGGT GACAACATCG GTGCTTATT	540
ACGTGGTGT GCACGTGAAG ACGTACAACG TGGACAAGTA TTAGCAGCTC CTGGCTCTAT	600
TACTCCACAC ACAAAATTCA AAGCTGATGT TTACGTTTA TCTAAAGAAG AAGGTGGACG	660
TCATACTCCA TTCTTCACTA ACTACCGCCC ACAATTCTAC TTCCGTACTA CTGACGTAAC	720
TGGCGTTGTT CACTTACCAAG AAGGTACTGA AATGGTTATG CCTGGCGATA ACGTAGAAAT	780
GAATGTTGAA TTGATCGCTC CAATCGCGAT TGAAGAC	817

## (2) INFORMATION FOR SEQ ID NO: 144:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus agalactiae*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

CGGAGCTATC CTTGTAGTTG CTTCAACTGA TGGACCAATG CCACAAACTC GTGAGCACAT	60
CCTTCTTCA CGTCAAGTTG GTGTTAAACA CCTTATCGTA TTCATGAACA AAGTTGACCT	120
TGTTGATGAT GAAGAATTGC TTGAATTGGT TGAAATGGAA ATTCGTGACC TTCTTCAGA	180
ATACGACTTC CCAGGTGATG ACCTTCCAGT TATCCAAGGT TCAGCTCTTA AAGCACTTGA	240
AGGCACGAA AAATACGAAG ACATCATCAT GGAATTGATG AGCACTGTTG ATGAGTACAT	300
TCCAGAACCA GAACGTGATA CTGACAAACC TTTACTTCTT CCAGTTGAAG ATGTATTCTC	360
AATCACTGGA CGTGGTACAG TTGCTTCAGG ACGTATCGAC CGTGGTACTG TTCGTGTCAA	420
CGACGAAGTT GAAATCGTTG GTATTAAGA AGATATCCAA AAAGCAGTTG TTACTGGTGT	480
TGAAATGTT CGTAAACAAAC TTGACGAAGG TCTTGCAGGG GACAACGTTG GTGTTCTCT	540
TCGTGGTGTGTT CAACGTGATG AAATCGAACG TGGTCAAGTT CTTGCTAAC CAGGTTCAAT	600

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CAACCCACAC ACTAAATTAA AAGGTGAAGT TTACATCCTT TCTAAAGAAG AAGGTGGACG	660
TCATACTCCA TTCTTCAACA ACTACCGTCC ACAATTCTAC TTCCGTACAA CTGACGTAAC	720
AGGTTCAATC GAACTTCCAG CAGGAACAGA AATGGTTATG CCTGGTGATA ACGTTACTAT	780
CGAAGTTGAA TTGATTCAACC CAATGCCGT AGAACAA	817

## (2) INFORMATION FOR SEQ ID NO: 145:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus pneumoniae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

CGGAGCTATC CTTGTAGTAG CTTCAACTGA CGGACCAATG CCACAAACTC GTGAGCACAT	60
CCTTCTTCA CGTCAGGTTG GTGTTAAACA CCTTATCGTC TTCATGAACA AAGTTGACTT	120
GGTTGACGAC GAAGAATTGC TTGAATTGGT TGAAATGGAA ATCCGTGACC TATTGTCAGA	180
ATACGACTTC CCAGGTGACG ATCTTCCAGT TATCCAAGGT TCAGCACTTA AAGCTCTTGA	240
AGGTGACTCT AAATACGAAG ACATCGTTAT GGAATTGATG AACACAGTTG ATGAGTATAT	300
CCCAGAACCA GAACGTGACA CTGACAAACC ATTGCTTCTT CCAGTCGAGG ACGTATTCTC	360
AATCACTGGA CGTGGTACAG TTGCTTCAGG ACGTATCGAC CGTGGTATCG TTAAAGTCAA	420
CGACGAAATC GAAATCGTTG GTATCAAAGA AGAAACTCRA AAAGCAGTTG TTACTGGTGT	480
TGAAATGTTT CGTAAACAAAC TTGACGAAGG TCTTGCTGGA GATAACGTAG GTGTCCTTCT	540
TCGTGGTGTGTT CAACGTGATG AAATCGAACG TGGACAAGTT ATCGCTAAC CAGGTTCAAT	600
CAACCCACAC ACTAAATTCA AAGGTGAAGT CTACATCCTT ACTAAAGAAG AAGGTGGACG	660
TCACACTCCA TTCTTCAACA ACTACCGTCC ACAATTCTAC TTCCGTACTA CTGACGTTAC	720
AGGTTCAATC GAACTTCCAG CAGGTACTGA AATGGTAATG CCTGGTGATA ACGTGACAAT	780
CGACGTTGAG TTGATTCAACC CAATGCCGT AGAACAA	817

## (2) INFORMATION FOR SEQ ID NO: 146:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid

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(C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:  
 (A) ORGANISM: *Streptococcus salivarius*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

CGGTGCGATC CTTGTAGTAG CATCTACTGA CGGACCAATG CCACAAACTC GTGAGCACAT	60
CCTTCCTTCA CGTCAGGTTG GTGTTAAACA CCTTATCGTC TTCATGAACA AAGTTGACTT	120
GGTTGACGAT GAAGAATTGC TTGAATTGGT TGAAATGGAA ATCCGTGACC TTCTTCAGA	180
ATACGATTTC CCAGGTGATG ACATTCCAGT TATCCAAGGT TCAGCTCTTA AAGCTCTTGA	240
AGGTGATTCT AAATACGAAG ACATCATCAT GGACTTGATG AACACTGTTG ACGAATACAT	300
CCCAGAACCA GAACGTGACA CTGACAAACC ATTGTTGCTT CCAGTCGAAG ACGTATTCTC	360
AATCACTGGT CGTGGTACTG TTGCTTCAGG ACGTATCGAC CGTGGTGTG TTCGTGTCAA	420
TGACGAAGTT GAAATCGTTG GTCTTAAAGA AGACATCCAA AAAGCAGTTG TTACTGGTGT	480
TGAAATGTT CGTAAACAAAC TTGACGRAGG TATTGCCGGA GATAACGTCG GTGTTCTTCT	540
TCGTGGTATC CAACGTGATG AAATCGAACG TGGTCAAGTA TTGGCTGCAC CTGGTTCAAT	600
CAACCCACAC ACTAAATTCA AAGGTGAAGT TTACATCCTT TCTAAAGAAG AAGGTGGACG	660
TCACACTCCA TTCTCAACA ACTACCGTCC ACAGTTCTAC TTCCGTACAA CTGACGTAAC	720
AGGTTCAATC GAACTTCCTG CAGGTACTGA AATGGTTATG CCTGGTGATA ACGTGACTAT	780
CGACGTTGAG TTGATCCACC CAATGCCGT TGAACAA	817

(2) INFORMATION FOR SEQ ID NO: 147:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 897 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:  
 (A) ORGANISM: *Agrobacterium tumefaciens*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:

AACATGATCA CCGGTGCTGC CGAGATGGAC GGCGCGATCC TGGTTGCTC GGCTGCCGAC	60
GGCCCGATGC CACAGACCCG CGAGCACATC CTGCTTGCCC GTCAGGTGGG CGTTCCGGCC	120

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ATCGTCGTGT	TCCTCAACAA	GGTCGACCAAG	GTTGACGACG	CCGAGCTTCT	CGAGCTCGTC	180
GAGCTTGAAG	TTCGCGAACT	TCTGTCGTCC	TACGACTTCC	CGGGCGACGA	TATCCCGATC	240
ATCAAGGGTT	CGGCACTTGC	TGCTCTTGAA	GATTCTGACA	AGAAGATCGG	TGAAGACGCG	300
ATCCGCGAGC	TGATGGCTGC	TGTCGACGCC	TACATCCCGA	CGCCTGAGCG	TCCGATCGAC	360
CAGCCGTTCC	TGATGCCGAT	CGAAGACGTG	TTCTCGATCT	CGGGTCGTGG	TACGGTTGTG	420
ACGGGTCGCG	TTGAGCGCGG	TATCGTCAAG	GTTGGTGAAG	AAGTCGAAAT	CGTCGGCATC	480
CGTCCGACCT	CGAAGACGAC	TGTTACCGGC	GTTGAAATGT	TCCGCAAGCT	GCTCGACCAG	540
GGCCAGGCCG	GCGACAACAT	CGGTGCACTC	GTTCGCGGGG	TTACCCGTGA	CGGCGTCGAG	600
CGTGGTCAGA	TCCTGTGCAA	GCCGGGTTCG	GTCAAGCCGC	ACAAGAAGTT	CATGGCAGAA	660
GCCTACATCC	TGACGAAGGA	AGAAGGCGGC	CGTCATACGC	CGTTCTTCAC	GAACCTACCGT	720
CCGCAGTTCT	ACTTCCGTAC	GACTGACGTT	ACCGGTATCG	TTTCGCTTCC	TGAAGGCACG	780
GAAATGGTTA	TGCCTGGCGA	CAACGTCACT	GTTGAAGTCG	AGCTGATCGT	TCCGATCGCG	840
ATGGAAGAAA	AGCTGCGCTT	CGCTATCCGC	GAAGGCGGCC	GTACCGTCGG	CGCCGGC	897

## (2) INFORMATION FOR SEQ ID NO: 148:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 885 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Bacillus subtilis*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

ATGATCACTG	GTGCTGCGCA	AATGGACGGA	GCTATCCTTG	TAGTATCTGC	TGCTGATGGC	60
CCAATGCCAC	AAACTCGTGA	GCACATCCTT	CTTTCTAAAA	ACGTTGGTGT	ACCATACATC	120
GTTGTATTCT	TAAACAAATG	CGACATGGTA	GACGACGAAG	AGCTTCTTGA	ACTAGTTGAA	180
ATGGAAGTTC	GCGATCTTCT	TAGCGAATAC	GACTTCCCTG	GTGATGATGT	ACCAGTTGTT	240
AAAGGTTCTG	CTCTTAAAGC	TCTTGAAGGA	GACGCTGAGT	GGGAAGCTAA	AATCTTCGAA	300
CTTATGGATG	CGGTTGATGA	GTACATCCCA	ACTCCAGAAC	GCGACACTGA	AAAACCATTG	360
ATGATGCCAG	TTGAGGACGT	ATTCTCAATC	ACTGGTCGTG	GTACAGTTGC	TACTGGCCGT	420
GTAGAACGCG	GACAAGTTAA	AGTCGGTGAC	GAAGTTGAAA	TCATCGGTCT	TCAAGAAGAG	480

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AACAAGAAAA CAACTGTTAC AGGTGTTGAA ATGTTCCGTA AGCTTCTTGA TTACGCTGAA	540
GCTGGTGACA ACATTGGTGC CCTTCTTCGC GGTGTATCTC GTGAAGAAAT CCAACGTGGT	600
CAAGTACTTG CTAAACCAGG TACAATCACT CCACACAGCA AATTCAAAGC TGAAGTTTAC	660
GTTCTTCTA AAGAAGAGGG TGGACGTCAT ACTCCATTCT TCTCTAACTA CCGTCCTCAG	720
TTCTACTTCC GTACAACTGA CGTAACTGGT ATCATCCATC TTCCAGAAGG CGTAGAAATG	780
GTTATGCCTG GAGATAACAC TGAAATGAAC GTTGAACCTA TTTCTACAAT CGCTATCGAA	840
GAAGGAACTC GTTTCTCTAT TCGTGAAGGC GGACGTACTG TTGGT	885

## (2) INFORMATION FOR SEQ ID NO: 149:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 882 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Bacteroides fragilis*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:

ATGGTTACTG GTGCTGCTCA GATGGACGGT GCTATCATTG TAGTTGCTGC TACTGATGGT	60
CCGATGCCTC AGACTCGTGA GCACATCCTT TTGGCTCGTC AGGTAAACGT TCCGAAGCTG	120
GTTGTATTCA TGAACAAGTG CGATATGGTT GAAGATGCTG AGATGTTGGA ACTTGTGAA	180
ATGGAAATGA GAGAATTGCT TTCATTCTAT GATTCGACG GTGACAATAC TCCGATCATT	240
CAGGGTTCTG CTCTTGGTGC ATTGAACGGC GTAGAAAAAT GGGAAAGACAA AGTAATGGAA	300
CTGATGGAAG CTGTTGATAC TTGGATTCCA CTGCCTCCGC GCGATGTTGA TAAACCTTC	360
TTGATGCCGG TAGAAGACGT GTTCTCTATC ACAGGTCGTG GTACTGTAGC TACAGGTCGT	420
ATCGAAACTG GTGTTATCCA TGTAGGTGAT GAAATCGAAA TCCTCGGTTT GGGTGAAGAT	480
AAGAAATCAG TTGTAACAGG TGTGAAATG TTCCGCAAAC TTCTGGATCA GGGTGAAGCT	540
GGTGACAAACG TAGGTCTGTT GCTTCGTGGT GTTGACAAGA ACGAAATCAA ACGTGGTATG	600
GTTCTTTGTA AACCGGGTCA GATTAAACCT CACTCTAAAT TCAAAGCAGA GGTTTATATC	660
CTGAAGAAAG AAGAAGGTGG TCGTCACACT CCATTCCATA ACAAAATATCG TCCTCAGTTC	720
TACCTGCGTA CTATGGACTG TACAGGTGAA ATCACTCTTC CGGAAGGAAC TGAAATGGTA	780
ATGCCGGGTG ATAACGTAAC TATCACTGTA GAGTTGATCT ATCCGGTTGC ACTGAACATC	840

GGTCTTCGTT TCGCTATCCG CGAAGGTGGA CGTACAGTAG GT

882

## (2) INFORMATION FOR SEQ ID NO: 150:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 888 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Borrelia burgdorferi*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

AATATGATTA CAGGAGCAGC TCAAATGGAT GCAGCGATAC	60
TTTTAGTTGC TGCTGATAGT	
GGTGCTGAGC CTCAAACAAA AGAGCATTG CTTCTTGCTC	120
AAAGAATGGG AATAAAGAAA	
ATAATAGTTT TTTTAAATAA ATTGGACTTA GCAGATCCTG	180
AACTTGTGA GCTTGTGAA	
GTTGAAGTTT TAGAACTTGT TGAAAAATAT GGCTTTCAAG	240
CTGATACTCC AATAATCAAA	
GGTCAGCTT TTGGGGCTAT GTCAAATCCA GAAGATCCTG	300
AATCTACAAA ATGCGTTAAA	
GAACTTCTTG AATCTATGGA TAATTATTTT GATCTTCCAG	360
AAAGAGATAT TGACAAGCCA	
TTTTGCTTG CTGTTGAAGA TGTATTTCT ATTCAGGAA GAGGCAGTGT	420
TGCTACTGGG	
CGTATTGAAA GAGGTATTAT TAAAGTTGGT CAAGAAGTTG	480
AAATAGTTGG AATTAAAGAA	
ACCAGAAAAA CTACTGTTAC TGGTGTGAA ATGTTCCAGA	540
AAATTCTTGA GCAAGGTCAA	
GCAGGGGATA ATGTTGGTCT TCTTTGAGA GGCAGTGATA	600
AAAAAGACAT TGAGAGGGGG	
CAAGTTTGT CAGCTCCAGG TACAATTACT CCACACAAGA	660
AATTAAAGC TTCAATTAT	
TGTTTACTA AAGAAGAAGG CGGTAGGCAC AAGCCATTT	720
TCCCAGGGTA TAGACCACAG	
TTCTTTTTA GAACAACCGA TGTTACTGGA GTTGTGCTT	780
TAGAGGGCAA AGAAATGGTT	
ATGCCTGGTG ATAATGTTGA TATTATTGTT GAGCTGATCT	840
CTTCAATAGC TATGGATAAG	
AATGTAGAAT TTGCTGTTCG AGAAGGTGGA AGAACCGTTG	888
CTTCAGGA	

## (2) INFORMATION FOR SEQ ID NO: 151:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 894 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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## (vi) ORIGINAL SOURCE:

(A) ORGANISM: *Brevibacterium linens*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

AACATGATCA CCGGTGCCGC TCAGATGGAC GGTGCGATCC TCGTCGTCGC CGCTACCGAC	60
GGACCGATGC CCCAGACCCG TGAGCACGTG CTGCTCGCGC GTCAGGTCGG CGTTCCCTAC	120
ATCGTCGTGG CTCTGAACAA GTCCGACATG GTCGATGACG AGGAGCTCCT CGAGCTCGTC	180
GAATTCGAGG TCCGCGACCT GCTCTCGAGC CAGGACTTCG ACGGAGACAA CGCTCCGGTC	240
ATTCCGGTGT CCGCTCTCAA GGCGCTGGAA GGCGACGAGA AGTGGGTCAA GAGCGTTCA	300
GATCTCATGG CTGCCGTGCA TGACAACGTT CCGGAGCCGG AGCGCGATGT CGACAAGCCG	360
TTCCTCATGC CCGTCGAGGA CGTCTTCACG ATCACCGGTC GTGGAACCGT CGTCACCGGT	420
CGTGTGAGC GCGGCCTGCT CCTGCCTAAC GACGAAATCG AAATCGTCGG CATCAAGGAG	480
AAGTCGTCCA AGACGACTGT CACCGCTATC GAGATGTTCC GCAAGACCT GCCGGATGCC	540
CGTGCAGGTG AGAACGTCGG TCTGCTCCTC CGCGGCACCA AGCGCGAGGA TGTTGAGCGC	600
GGTCAGGTCA TCGTGAAGCC GGGTCGATC ACCCCGCACA CCAAGTTCGA GGTCAGGTCA	660
TACATCCTGA GCAAGGACGA GGGCGGACGT CACAACCCGT TCTACTCGAA CTACCGTCCG	720
CAGTTCTACT TCCGGACCAC GGACGTCACC GGTGTCATCA CGCTGCCGA GGGCACCGAG	780
ATGGTCATGC CCGGCACAA CACCGATATG TCGGTGAGC TCATCCAGCC GATCGCTATG	840
GAGGACCGCC TCCGCTTCGC AATCCCGAA GGTGGCCGCA CCGTCGGCGC CGGT	894

## (2) INFORMATION FOR SEQ ID NO: 152:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 888 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

(A) ORGANISM: *Burkholderia cepacia*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

ATGATCACGG GCGCAGCGCA GATGGACGGC GCGATCCTGG TTTGCTCGGC AGCAGACGGC	60
CCGATGCCGC AAACGCGTGA GCACATCCTG CTGGCGCGTC AGGTTGGTGT TCCGTACATC	120
ATCGTGTTCG TGAACAAAGTG CGACAGTGTG GACGACGGCTG AACTGCTCGA GCTGGTCGAG	180

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ATGGAAGTTC GCGAACTCCT GTCGAAGTAC GACTTCCCGG GCGACGACAC GCCGATCGT	240
AAGGGTTCGG CCAAGCTGGC GCTGGAAGGC GACACGGGCG AGCTGGCGA AGTGGCGATC	300
ATGAGCCTGG CAGACCGCGCT GGACACGTAC ATCCCGACGC CGGAGCGTGC AGTTGACGGC	360
GCGTTCTGA TGCCGGTGGA AGACGTGTT CCGATCTCGG GCCGTGGTAC GGTGGTGACG	420
GGTCGTGTCG AGCGCGGCAT CGTGAAGGTC GGCGAAGAAA TCGAAATCGT CGGTATCAAG	480
CCGACGGTGA AGACGACCTG CACGGCGTT GAAATGTTCC GCAAGCTGCT GGACCAAGGT	540
CAGGCAGGCG ACAACGTCGG TATCCTGCTG CGCGGCACGA AGCGTGAAGA CGTGGAGCGT	600
GGCCAGGGTTC TGGCGAAGCC GGGTTCGATC ACGCCGCACA CGCACTTCAC GGCTGAAGTG	660
TACGTGCTGA GCAAGGACGA AGGCAGGCCGT CACACGCCGT TCTTCAACAA CTACCGTCCG	720
CAGTTCTACT TCCGTACGAC GGACGTGACG GGCTCGATCG AGCTGCCGAA GGACAAGGAA	780
ATGGTGATGC CGGGCGACAA CGTGTGATC ACGGTGAAGC TGATTGCTCC GATCGCGATG	840
GAAGAAGGTC TGCGCTTCGC AATCCGTGAA GGCGGCCGTA CGGTCGGC	888

## (2) INFORMATION FOR SEQ ID NO: 153:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Chlamydia trachomatis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

AACATGATCA CCGGTGCGGC TCAAATGGAC GGGGCTATTG TAGTAGTTTC TGCAACAGAC	60
GGAGCTATGC CTCAAACCAA AGAGCATATT CTTTTGGCAA GACAAGTTGG GGTTCCCTAC	120
ATCGTTGTTT TTCTCAATAA AATTGACATG ATTTCCGAAG AAGACGCTGA ATTGGTCGAC	180
TTGGTTGAGA TGGAGTTGGC TGAGCTTCTT GAAGAGAAAG GATACAAAGG GTGTCCAATC	240
ATCAGAGGTT CTGCTCTGAA AGCTTGGAA GGAGATGCTG CATACTAGA GAAAGTTCGA	300
GAGCTAATGC AAGCCGTCCA TGATAATATC CCTACTCCAG AAAGAGAAAT TGACAAGCCT	360
TTCTTAATGC CTATTGAGGA CGTGTCTCT ATCTCCGGAC GAGGAACGT AGTAACGTGGA	420
CGTATTGAGC GTGGAATTGT TAAAGTTCC GATAAAAGTTC AGTTGGTCGG TCTTAGAGAT	480
ACTAAAGAAA CGATTGTTAC TGGGGTTGAA ATGTTCAGAA AAGAACTCCC AGAAGGTGCGT	540

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GCAGGAGAGA ACGTTGGATT GCTCCTCAGA GGTATTGGTA AGAACGATGT GGAAAGAGGA	600
ATGGTTGTTT GCTTGCCAAA CAGTGTAAA CCTCATAACAC AGTTAACGTG TGCTGTTTAC	660
GTTCTGCAA AAGAAGAAGG TGGACGACAT AAGCCTTCT TCACAGGATA TAGACCTCAA	720
TTCTTCTTCC GTACAACAGA CGTTACAGGT GTGGTAACTC TGCCTGAGGG AGTTGAGATG	780
GTCATGCCTG GGGATAACGT TGAGTTGAA GTGCAATTGA TTAGCCCTGT GGCTTTAGAA	840
GAAGGTATGA GATTTCGAT TCGTGAAGGT GGTCGTACAA TCGGTGCTGG A	891

## (2) INFORMATION FOR SEQ ID NO: 154:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Escherichia coli*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

AACATGATCA CCGGTGCTGC GCAGATGGAC GGCGCGATCC TGGTAGTTGC TGCGACTGAC	60
GGCCCGATGC CGCAGACTCG TGAGCACATC CTGCTGGTC GTCAGGTAGG CGTTCCGTAC	120
ATCATCGTGT TCCTGAACAA ATGCGACATG GTTGATGACG AAGAGCTGCT GGAACTGGTT	180
GAAATGGAAG TTCGTGAAC TCTGTCTCAG TACGACTTCC CGGGCGACGA CACTCCGATC	240
GTTCGTGGTT CTGCTCTGAA AGCGCTGGAA GGCGACGCAG AGTGGGAAGC GAAAATCCTG	300
GAACCTGGCTG GCTTCCTGGA TTCTTACATT CCGGAACCAG AGCGTGCAGTGACAAAGCCG	360
TTCCCTGCTGC CGATCGAAGA CGTATTCTCC ATCTCCGGTC GTGGTACCGT TGTTACCGGT	420
CGTGTAGAAC GCGGTATCAT CAAAGTTGGT GAAGAAGTTG AAATCGTTGG TATCAAAGAG	480
ACTCAGAAAGT CTACCTGTAC TGGCGTTGAA ATGTTCCGCA AACTGCTGGA CGAAGGCCGT	540
GCTGGTGAGA ACGTAGGTGT TCTGCTGCAG GGTATCAAAC GTGAAGAAAT CGAACGTGGT	600
CAGGTACTGG CTAAGCCGGG CACCATCAAG CCGCACACCA AGTCGAATC TGAAGTGTAC	660
ATTCTGTCCA AAGATGAAGG CGGCCGTCA ACTCCGTTCT TCAAAGGCTA CCGTCCGCAG	720
TTCTACTTCC GTACTACTGA CGTGACTGGT ACCATCGAAC TGCCGGAAGG CGTAGAGATG	780
GTAATGCCGG GCGACAACAT CAAAATGGTT GTTACCCCTGA TCCACCCGAT CGCGATGGAC	840
GACGGTCTGC GTTTCGCAAT CCGTGAAGGC GGCGTACCG TTGGCGCGGG C	891

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## (2) INFORMATION FOR SEQ ID NO: 155:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Fibrobacter succinogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:

AACATGGTGA	CTGGTGCTGC	TCAGATGGAC	GGCGCTATCC	TCGTTGTTGC	CGCTACTGAC	60
GGTCCGATGC	CGCAGACTCG	CGAACACATC	CTTCTCGCTC	ACCAGGTTGG	CGTGCCGAAG	120
ATCGTCGTGT	TCATGAACAA	GTGCGACATG	GTTGACGATG	CTGAAATTCT	CGACCTCGTC	180
GAAATGGAAG	TTCGCGAACT	CCTCTCCAAG	TATGACTTCG	ACGGTGACAA	CACCCCGATC	240
ATCCGTGGTT	CCGCTCTCAA	GGCCCTCGAA	GGCGATCCGG	AATACCAGGA	CAAGGTCATG	300
GAACTCATGA	ACGCTTGCAG	CGAACATACATC	CCGCTCCCGC	AGCGCGATAC	CGACAAGCCG	360
TTCCCTCATGC	CGATCGAAGA	CGTGGTCACG	ATTACTGGCC	GCGGCACTGT	CGCTACTGGC	420
CGTATCGAAC	GCGGTGTCGT	TCGCTTGAAC	GACAAGGTTG	AACGTATCGG	TCTCGGTGAA	480
ACCACCGAAT	ACGTCATCAC	CGGTGTTGAA	ATGTTCCGTA	AGCTCCTCGA	CGACGCTCAG	540
GCAGGGTACA	ACGTTGGTCT	CCTCCTCCGT	GGTGCTGAAA	AGAAGGACAT	CGTCCGTGGC	600
ATGGTTCTCG	CAGCTCCGAA	GTCTGTCACT	CCGCACACCG	AATTAAAGGC	TGAAATCTAC	660
GTTCTCACGA	AGGACGAAGG	TGGCCGTCAC	ACGCCGTTCA	TGAATGGCTA	CCGTCCGCAG	720
TTCTACTTCC	GCACCACCGA	CGTTACTGGT	ACGATCCAGC	TCCCGGAAGG	TGTCGAAATG	780
GTTACTCCGG	GTGACACGGT	CACGATCCAC	GTGAACCTCA	TCGCTCCGAT	CGCTATGGAA	840
AAGCAGCTCC	GCTTCGCTAT	CCGTGAAGGT	GGACGTACTG	TTGGTGCTGG	C	891

## (2) INFORMATION FOR SEQ ID NO: 156:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 894 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Flavobacterium ferrugineum*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

AACATGATCA CCGGTGCTGC CCAGATGGAC GGTGCTATCT TAGTTGTGGC TGCATCAGAC	60
GGTCCTATGC CTCAAACAAA AGAACACATC CTGCTTGCTG CCCAGGTAGG TGTACCTAAA	120
ATGGTTGTGT TTCTGAATAA AGTTGACCTC GTTGACGACG AAGAGCTCCT GGAGCTGGTT	180
GAGATCGAGG TTCGCGAAGA ACTGACTAAA CGCGGTTTCG ACGGCGACAA CACTCCAATC	240
ATCAAAGGTT CCGCTACAGG CGCCCTCGCT GGTGAAGAAA AGTGGGTTAA AGAAATTGAA	300
AACCTGATGG ACGCTGTTGA CAGCTACATC CCACTGCCTC CTCGTCCGGT TGATCTGCCG	360
TTCCTGATGA GCGTAGAGGA CGTATTCTCT ATCACTGGTC GTGGTACTGT TGCTACCGGT	420
CGTATCGAGC GTGGCCGTAT CAAAGTTGGT GAGCCTGTTG AGATCGTAGG TCTGCAGGAG	480
TCTCCCTGA ACTCTACCGT TACAGGTGTT GAGATGTTCC GCAAACTCCT CGACGAAGGT	540
GAAGCTGGTG ATAACGCCGG TCTCCTCCTC CGTGGTGTG AAAAAACACA GATCCGTCGC	600
GGTATGGTAA TCGTTAACCC CGGTTCCATC ACTCCGCACA CGGACTTCAA AGGCGAAGTT	660
TACGTACTGA GCAAAGACGA AGGTGGCCGT CACACTCCAT TCTTCAACAA ATACCGTCCT	720
CAATTCTACT TCCGTACAAC TGACGTTACA GGTGAAGTAG AACTGAACGC AGGAACAGAA	780
ATGGTTATGC CTGGTGATAA CACCAACCTG ACCGTTAACAC TGATCCAACC GATCGCTATG	840
GAAAAAGGTC TGAAATTCGC GATCCCGAA GGTGGCCGTA CCGTAGGTGC AGGA	894

## (2) INFORMATION FOR SEQ ID NO: 157:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Haemophilus influenzae*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

AATATGATTA CTGGTGCAGGC ACAAAATGGAT GGTGCTATTT TAGTAGTAGC AGCAACAGAT	60
GGTCCTATGC CACAAACTCG TGAACACATC TTATTAGGTC GCCAAGTAGG TGTTCCATAC	120
ATCATCGTAT TCTTAAACAA ATGCGACATG GTAGATGACG AAGAGTTATT AGAATTAGTC	180
GAAATGGAAG TTCGTGAAC TCTATCTCAA TATGACTTCC CAGGTGACGA TACACCAATC	240

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GTACGTGGTT CAGCATTACA AGCGTTAAC GGC GTAGCAG AATGGGAAGA AAAAATCCTT	300
GAGTTAGCAA ACCACTTAGA TACTTACATC CCAGAACCGAG AACGTGCGAT TGACCAACCG	360
TTCCTTCTTC CAATCGAAGA TGTGTTCTCA ATCTCAGGTC GTGGTACTGT AGTAACAGGT	420
CGTGTAGAAC GAGGTATTAT CCGTACAGGT GATGAAGTAG AAATCGTCGG TATCAAAGAT	480
ACAGCGAAAA CTACTGTAAC GGGTGTGAA ATGTTCCGTA AATTACTTGA CGAAGGTCGT	540
GCAGGTGAAA ACATCGGTGC ATTATTACGT GGTACCAAAC GTGAAGAAAT CGAACGTGGT	600
CAAGTATTAG CGAAACCAGG TTCAATCACA CCACACACTG ACTTCGAATC AGAAGTGTAC	660
GTATTATCAA AAGATGAAGG TGGTCGTCA ACTCCATTCT TCAAAGGTTA CCGTCCACAA	720
TTCTATTCGTACACAACAGA CGTGACTGGT ACAATCGAAT TACCAGAAGG CGTGGAAATG	780
GTAATGCCAG GCGATAACAT CAAGATGACA GTAAGCTAA TCCACCCAAT TGCGATGGAT	840
CAAGGTTTAC GTTTCGCAAT CCGTGAAGGT GGCGTACAG TAGGTGCAGG C	891

## (2) INFORMATION FOR SEQ ID NO: 158:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 906 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Helicobacter pylori*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

AACATGATCA CCGGTGCGGC GCAAATGGAC GGAGCGATTT TGGTTGTTTC TGCAGCTGAT	60
GGCCCTATGC CTCAAACTAG GGAGCATATC TTATTGTCTC GTCAAGTAGG CGTGCCTCAC	120
ATCGTTGTTT TCTTAAACAA ACAAGACATG GTAGATGACC AAGAATTGTT AGAACTTGTAA	180
GAAATGGAAG TGCGCGAATT GTTGAGCGCG TATGAATTTC CTGGCGATGA CACTCCTATC	240
GTAGCGGGTT CAGCTTAAAG AGCTTAGAA GAAGCAAAGG CTGGTAATGT GGGTGAATGG	300
GGTGAAAAAG TGCTTAAACT TATGGCTGAA GTGGATGCCT ATATCCCTAC TCCAGAAAGA	360
GACACTGAAA AAACTTCTT GATGCCGGTT GAAGATGTGT TCTCTATTGC GGGTAGAGGG	420
ACTGTGGTTA CAGGTAGGAT TGAAAGAGGC GTGGTGAAAG TAGGCATGA AGTGGAAATC	480
GTTGGTATCA GACCTACACA AAAAACGACT GTAACCCTGT TAGAAATGTT TAGGAAAGAG	540
TTGGAAAAAG GTGAAGCCGG CGATAATGTG GGC GTGCTTT TGAGAGGAAC TAAAAAAGAA	600

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GAAGTGGAAC GCGGTATGGT TCTATGAAA CCAGGTTCTA TCACTCCGCA CAAGAAATT	660
GAGGGAGAAA TTTATGTCCT TTCTAAAGAA GAAGGCGGGA GACACACTCC ATTCTTCACC	720
AATTACCGCC CGCAATTCTA TGTGCGACA ACTGATGTGA CTGGCTCTAT CACCCCTCCT	780
GAAGGCGTAG AAATGGTTAT GCCTGGCGAT AATGTGAAAA TCACTGTAGA GTTGATTAGC	840
CCTGTTGCGT TAGAGTTGGG AACTAAATT GCGATTCGTG AAGGCGGTAG GACCGTTGGT	900
GCTGGT	906

(2) INFORMATION FOR SEQ ID NO: 159:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Micrococcus luteus*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

AACATGATCA CCGCGGCCGC TCAGATGGAC GGCGCGATCC TCGTGGTCGC CGCTACCGAC	60
GGCCCGATGG CCCAGACCCG TGAGCACGTG CTCCTGGCCC GCCAGGTCGG CGTGCCGGCC	120
CTGCTCGTGG CCCTGAACAA GTCGGACATG GTGGAGGACG AGGAGCTCCT CGAGCGTGTG	180
GAGATGGAGG TCCGGCAGCT GCTGTCCTCC AGGAGCTTCG ACGTCGACGA GGCCCCGGTC	240
ATCCGCACCT CCGCTCTGAA GGCCCTCGAG GGCGACCCCC AGTGGGTCAA GTCCGTCGAG	300
GACCTCATGG ATGCCGTGGA CGAGTACATC CCGGACCCGG TGCGCGACAA GGACAAGCCG	360
TTCCCTGATGC CGATCGAGGA CGTCTTCACG ATCACCGGCC GTGGCACCGT GGTGACCGGT	420
CGCGCCGAGC GCGGCACCCCT GAAGATCAAC TCCGAGGTCG AGATCGTCGG CATCCGCGAC	480
GTGCAGAAGA CCACTGTAC CGGCATCGAG ATGTTCCACA AGCAGCTCGA CGAGGCCTGG	540
GCCGGCGAGA ACTGCGGTCT GCTCGTGCAC GGTCTGAAGC GCGACGACGT CGAGCGCGGC	600
CAGGTGCTGG TGGAGCCGGG CTCCATCACC CCGCACACCA ACTTCGAGGC GAACGTCTAC	660
ATCCTGTCCA AGGACGAGGG TGGGCGTCAC ACCCCGTTCT ACTCGAACTA CCGCGCGCAG	720
TTCTACTTCC GCACCACCGA CGTCACCGGC GTCATCACGC TGCCCGAGGG CACCGAGATG	780
GTCATGCCCG GCGACACCAAC CGAGATGTGCG GTCGAGCTCA TCCAGCCGAT CGCCATGGAG	840
GAGGGCCTCG GCTTCGCCAT CCGCGAGGGT GGCGCACCAG TGGGCTCCGG C	891

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## (2) INFORMATION FOR SEQ ID NO: 160:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Mycobacterium tuberculosis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

AACATGATCA CCGCGCCGC GCAGATGGAC GGTGCGATCC TGGTGGTCGC CGCCACCGAC	60
GGCCCGATGC CCCAGACCCG CGAGCACGTT CTGCTGGCGC GTCAAGTGGG TGTGCCCTAC	120
ATCCTGGTAG CGCTGAACAA GGCGACGCA GTGGACGACG AGGAGCTGCT CGAACTCGTC	180
GAGATGGAGG TCCCGAGCT GCTGGCTGCC CAGGAATTG ACGAGGACGC CCCGGTTGTG	240
CGGGTCTCGG CGCTCAAGGC GCTCGAGGGT GACCGAAGT GGGTTGCCTC TGTCGAGGAA	300
CTGATGAACG CGGTCGACGA GTCGATTCCG GACCCGGTCC GCGAGACCGA CAAGCCGTT	360
CTGATGCCGG TCGAGGACGT CTTCACCATT ACCGGCCGCG GAACCGTGGT CACCGGACGT	420
GTGGAGCGCG GCGTGATCAA CGTGAACGAG GAAGTTGAGA TCGTCGGCAT TCGCCCATCG	480
ACCACCAAGA CCACCGTCAC CGGTGTGGAG ATGTTCCGCA AGCTGCTCGA CCAGGGCCAG	540
CGGGGCGACA ACGTTGGTT GCTGCTGCGG GGCCTCAAGC GCGAGGACGT CGAGCGTGGC	600
CAGGTTGTCA CCAAGCCCGG CACCACACG CCGCACACCG AGTTCGAAGG CCAGGTCTAC	660
ATCCTGTCCA AGGACGAGGG CGGCCGGCAC ACGCCGTTCT TCAACAACTA CCGTCCGCAG	720
TTCTACTTCC GCACCAACCGA CGTGACCGGT GTGGTACAC TGCCGGAGGG CACCGAGATG	780
GTGATGCCCG GTGACAACAC CAACATCTCG GTGAAGTTGA TCCAGCCCGT CGCCATGGAC	840
GAAGGTCTGC GTTTCGCGAT CCGCGAGGGT GGCCGCACCG TGGGCGCCGG C	891

## (2) INFORMATION FOR SEQ ID NO: 161:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Mycoplasma genitalium*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

AATATGATCA CAGGTGCTGC ACAAAATGGAT GGAGCTATT TAGTTGTTTC AGCAACTGAT	60
AGTGTGATGC CCCAAACCCG CGAGCACATC TTACTGCCC GCCAAGTAGG GGTTCCCTAAA	120
ATGGTAGTTT TTCTAAACAA GTGTGATATT GCTAGTGATG AAGAGGTACA AGAACCTGTT	180
GCTGAAGAAG TACGTGATCT GTTAACITCC TATGGTTTG ATGGTAAGAA CACTCCTATT	240
ATTTATGGCT CAGCTTTAAA AGCATTGGAA GGTGATCCAA AGTGGGAGGC TAAGATCCAT	300
GATTGATTA AAGCAGTTGA TGAATGGATT CCAACTCCTA CACGTGAAGT AGATAAACCT	360
TTCTTATTAG CAATTGAAGA TACGATGACC ATTACTGGTA GAGGTACAGT TGTTACAGGA	420
AGAGTTGAAA GAGGTGAAC CAAAGTAGGT CAAGAAGTTG AAATTGTTGG TTTAAAACCA	480
ATTAGAAAAG CAGTTGTTAC TGGAATTGAA ATGTTCAAAA AGGAACCTGA TTCAGCAATG	540
GCTGGTGACA ATGCTGGGGT ATTATTACGT GGTGTTGAAC GTAAAGAAGT TGAAAGAGGT	600
CAAGTTTAG CAAAACCAGG CTCTATTAAA CCGCACAAAGA AATTAAAGC TGAGATCTAT	660
GCTTTAAAGA AAGAAGAAGG TGGTAGACAC ACTGGTTTT TAAACGGTTA CCGTCCTCAA	720
TTCTATTCC GTACCACTGA TGTAACCTGGT TCTATTGCTT TAGCTGAAAA TACTGAAATG	780
GTTCTACCTG GTGATAATGC TTCTATTACT GTTGAGTTAA TTGCTCCTAT CGCTTGTGAA	840
AAAGGTAGTA AGTCTCAAT TCGTGAAGGT GGTAGAACTG TAGGGGCAGG C	891

## (2) INFORMATION FOR SEQ ID NO: 162:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Neisseria gonorrhoeae*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

AACATGATTA CCGCGGCCGC ACAAAATGGAC GGTGCAATCC TGGTATGTT TGCTGCCGAC	60
GGCCCTATGC CGCAAACCCG CGAACACATC CTGCTGGCCC GTCAAGTAGG CGTACCTTAC	120
ATCATCGTGT TCATGAACAA ATGCGACATG GTCGACGATG CCGAGCTGTT CCAACTGGTT	180
GAAATGGAAA TCCCGCAGCT GCTGTCCAGC TACGACTTCC CCGGCACGA CTGCCCGATC	240

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GTACAAGGTT CCGCACTGAA AGCCTTGGAA GGCATGCCG CTTACGAAGA	AAAAATCTTC	300
GAACCTGGCTA CCGCATTGGA CAGATACATC CCGACTCCCG AGCGTGCCGT	GGACAAACCA	360
TTCCTGCTGC CTATCGAAGA CGTGTCTCC ATTTCCGGCC GCGGTACCGT	AGTCACCGGC	420
CGTGTAGAGC GAGGTATCAT CCACGTTGGT GACGAGATTG	AAATCGTCGG TCTGAAAGAA	480
ACCCAAAAAA CCACCTGTAC CGGCGTTGAA ATGTTCCGCA	AACTGCTGGA CGAAGGTCAG	540
GCAGGGCGACA ACGTAGGCCT ATTGCTGCAC	GGTACCAAAC GTGAAGACGT AGAACGCGGT	600
CAGGTATTGG CCAAACGGGG TACTATCACT CCTCACACCA	AGTTCAAAGC AGAAGTGTAC	660
GTATTGAGCA AAGAAGAGGG CGGCCCCAT ACCCCGTTT TCGCCAACTA	CCGTCCCCAA	720
TTCTACTTCC GTACCACTGA CGTAACCGGC ACGATTACTT	TGGAAAAAGG TGTGGAAATG	780
GTAATGCCGG GTGAGAACGT AACCATTACT GTAGAACTGA	TTGCGCCTAT CGCTATGGAA	840
GAAGGTCTGC GCTTGCGAT TCGCGAAGGC GGCGTACCG	TGGGTGCCGG C	891

## (2) INFORMATION FOR SEQ ID NO: 163:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Rickettsia prowazekii*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

AATATGATAA CTGGTGCCGC TCAGATGGAT GGTGCTATAT TAGTAGTTTC	TGCTGCTGAT	60
GGTCCTATGC CTCAAACTAG AGAACATATA TTACTGGCAA AACAGGTAGG	TGTACCTGCT	120
ATGGTAGTAT TTTGAATAA AGTAGATATG GTAGATGATC CTGACCTATT	AGAATTAGTT	180
GAGATGGAAG TAAGAGAATT ATTATCAAAA TATGGTTCC CTGGTAATGA	AATACCTATT	240
ATTAAAGGTT CTGCACTTCA AGCTTAGAA GGAAAACCTG AAGGTAAAAA	AGCTATTAAT	300
GAGTTAATGA ATGCAGTAGA TACGTATATA CCTCAGCCTA TAGAGCTACA	AGATAAACCT	360
TTTTTAATGC CAATAGAGGA TGTATTTCT ATTCAGGCA GAGGTACCGT	TGTAACTGGT	420
AGAGTGGAGT CAGGCATAAT TAAGGTGGGT GAAGAAATTG AAATAGTAGG	TCTAAAAAAT	480
ACGCAAAAAAA CGACTTGTAC AGGTGTAGAA ATGTTCAGAA AATTACTTGA	TGAAGGACAA	540
TCTGGAGATA ATGTCGGTAT ATTACTACGT GGTACAAAAA GAGAAGAAGT	AGAAAGAGGA	600

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CAAGTACTTG CAAAACCTGG GAGCATAAAA CCGCATGATA AATTTGAAGC TGAAGTGTAT	660
GTGCTTAGTA AAGAGGAAGG TGGACGTCAT ACCCCATTAA CTAATGATTA TCGCCCACAG	720
TTCTATTTA GAACAACAGA TGTTACCGGC ACAATAAAAT TGCCTCTGA TAAGCAGATG	780
GTTATGCCTG GAGATAATGC TACTTTTCA GTAGAATTAA TTAAGCCGAT TGCTATGCAA	840
GAAGGGTTAA AATTCTCTAT ACGTGAAGGT GGTAGAACAG TAGGAGCCGG T	891

## (2) INFORMATION FOR SEQ ID NO: 164:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Salmonella typhimurium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

AACATGATCA CCGGTGCTGC TCAGATGGAC GGCGCGATCC TGGTTGTTGC TGCGACTGAC	60
GGCCCGATGC CGCAGACCCG TGAGCACATC CTGCTGGTC GTCAGGTAGG CGTCCGTAC	120
ATCATCGTGT TCCTGAACAA ATGCGACATG GTTGATGACG AAGAGCTGCT GGAACTGGTT	180
GAGATGGAAG TTCGCGAACT GCTGTCTCAG TACGACTTCC CGGGCGACGA CACTCCGATC	240
GTTCGTGGTT CTGCTCTGAA AGCGCTGGAA GGCGACGCAG AGTGGGAAGC GAAAATCATC	300
GAACCTGGCTG GCTTCCTGGA TTCTTATATT CCGGAACCAG AGCGTGCAGAT TGACAAGCCG	360
TTCCCTGCTGC CGATCGAAGA CGTATTCTCC ATCTCCGGTC GTGGTACCGT TGTTACCGGT	420
CGTGTAGAGC GCGGTATCAT CAAAGTGGC GAAGAAGTTG AAATCGTTGG TATCAAAGAG	480
ACTCAGAAAGT CTACCTGTAC TGGCGTTGAA ATGTTCCGCA AACTGCTGGA CGAAGGCCGT	540
GCCGGTGAGA ACGTAGGTGT TCTGCTGCGT GGTATCAAAC GTGAAGAAAT CGAACGTGGT	600
CAGGTACTGG CTAAGCCGGG CACCATCAAG CCGCACACCA AGTCGAATC TGAAGTGTAC	660
ATTCTGTCCA AAGATGAAGG CGGCCGTCACTCCGTTCT TCAAAGGCTA CCGTCCGCAG	720
TTCTACTTCC GTACTACTGA CGTGACTGGT ACCATCGAAC TGCCGGAAGG CGTAGAGATG	780
GTAATGCCGG GCGACAACAT CAAAATGGTT GTTACCCCTGA TCCACCCGAT CGCGATGGAC	840
GACGGTCTGC GTTTCGCAAT CCGTGAAGGC GGCGTACCG TTGGCGCGGG C	891

## (2) INFORMATION FOR SEQ ID NO: 165:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 881 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Shewanella putida*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

ATGATCACTG GTGCTGCACA GATGGACGGC GCGATTCTGG TAGTCGCTTC AACAGACGGT	60
CCAATGCCAC AGACTCGTGA GCACATCCTG CTTTCTCGTC AGGTTGGCGT ACCATTCA	120
ATCGTATTCA TGAACAAATG TGACATGGTA GATGACGAAG AGCTGTTAGA GCTAGTTGAG	180
ATGGAAGTGC GTGAACTGTT ATCAGAATAC GATTTCCCAG GTGATGACTT ACCGGTAATC	240
CAAGGTTCACT CTCTGAAAGC GCTAGAAGGC GAGCCAGAGT GGGAAAGCAAA AATCCTTGAA	300
TTAGCAGCGG CGCTGGATTG TTACATTCCA GAACCACAAAC GTGACATCGA TAAGCCGTT	360
CTACTGCCAA TCGAAGACGT ATTCTCAATT TCAGGCCGTG GTACAGTAGT AACAGGTCGT	420
GTTGAGCGTG GTATTGTACG CGTAGGCGAC GAAGTTGAAA TCGTTGGTGT ACGTGCGACA	480
ACTAAGACAA CGTGTACTGG TGTAGAAATG TTCCGTAAAC TGCTTGACGA AGGTCGTGCA	540
GGTGAGAACT GTGGTATTTT GTTACGTGGT ACTAAGCGTG ATGACGTAGA ACGTGGTCAA	600
GTATTAGCGA AGCCAGGTTA AATCAACCCA CACACTACTT TTGAATCAGA AGTTTACGTA	660
CTGTCAAAAG AAGAAGGTGG TCGTCACACG CCATTCTTCA AAGGCTACCG TCCACAGTTC	720
TACTTCCGTA CAACTGACGT AACCGGTACT ATCGAACTGC CAGAAGGCGT AGAGATGGTA	780
ATGCCAGGCG ATAACATCAA GATGGTAGTG AACTGATTG GCCCAATCGC GATGGACGAA	840
GGTTTACGCT TCGCAATCCG TGAAGGCGGT CGTACAGTGG T	881

## (2) INFORMATION FOR SEQ ID NO: 166:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 897 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Stigmatella aurantiaca*

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## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

AACATGATCA CGGGCGCGGC GCAGATGGAC GGAGCGATTG	60
GGCCCGATGC CCCAGACGCG TGAGCACATC CTGCTGGCCA GGCAGGTGGG CGTGCCTAC	120
ATCGTCGTCT TCCTGAACAA GGTGGACATG CTGGACGATC CGGAGCTGCG CGAGCTGGT	180
GAGATGGAGG TGCAGCGACCT GCTCAAGAAG TACGAGTTCC CGGGCGACAG CATCCCCATC	240
ATCCCTGGCA GCGCGCTCAA GGCGCTGGAG GGAGACACCA GCGACATCGG CGAGGGAGCG	300
ATCCTGAAGC TGATGGCGGC GGTGGACGAG TACATCCGA CGCCGCAGCG TGCGACGGAC	360
AAGCCGTTCC TGATGCCGGT GGAAGACGTG TTCTCCATCG CAGGCCGAGG AACGGTGGCG	420
ACGGGCCGAG TGGAGCGCGG CAAGATCAAG GTGGGCGAGG AAGTGGAGAT CGTGGGGATC	480
CGTCCGACGC AGAAGACGGT CATCACGGGG GTGGAGATGT TCCGCAAGCT GCTGGACGAG	540
GGCATGGCGG GAGACAACAT CGGAGCGCTG CTGCGAGGCC TGAAGCGCGA GGACCTGGAG	600
CGTGGGCAGG TGCTGGCGAA CTGGGGGAGC ATCAACCCGC ACACGAAGTT CAAGGCGCAG	660
GTGTACGTGC TGTCGAAGGA AGAGGGAGGG CGGCACACGC CGTTCTCAA GGGATAACCGG	720
CCGCAGTTCT ACTTCCGGAC GACGGACGTG ACCGGAACGG TGAAGCTGCC GGACAACGTG	780
GAGATGGTGA TGCCGGGAGA CAACATCGCC ATCGAGGTGG AGCTCATTAC TCCGGTCGCC	840
ATGGAGAAGG AGCTGCCGTT CGCCATCCGT GAGGGTGGCC GCACGGTGGG CGCCGGC	897

## (2) INFORMATION FOR SEQ ID NO: 167:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 894 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus pyogenes*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167:

AACATGATCA CTGGTGCCGC TCAAATGGAC GGAGCTATCC TTGTAGTTGC TTCAACTGAT	60
GGACCAATGC CACAAACTCG TGAGCACATC CTTCTTCAC GTCAGGTTGG TGTTAACAC	120
CTTATCGTGT TCATGAACAA AGTTGACCTT GTTGATGACG AAGAGTTGCT TGAATTAGTT	180
GAGATGGAAA TTCGTGACCT TCTTTCAGAA TACGATTCC CAGGTGATGA CCTTCCAGTT	240
ATCCAAGGTT CAGCTCTTAA AGCTCTTGAA GCGGACACTA AATTGAAAGA CATCATCATG	300

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GAATTGATGG ATACTGTTGA TTCATACATT CCAGAACAG AACGCGACAC TGACAAACCA	360
TTGCTTCTTC CAGTCGAAGA CGTATTCTCA ATTACAGGTC GTGGTACAGT TGCTTCAGGA	420
CGTATCGACC GTGGTACTGT TCGTGTCAAC GACGAAATCG AAATCGTTGG TATCAAAGAA	480
GAAACTAAAA AAGCTGTTGT TACTGGTGT GAAATGTTCC GTAAACAACT TGACGAAGGT	540
CTTGCAGGAG ACAACGTAGG TATCCTCTT CGTGGTGTTC AACGTGACGA AATCGAACGT	600
GGTCAAGTTA TTGCTAAACC AAGTTCAATC AACCCACACA CTAAATTCAA AGGTGAAGTA	660
TATATCCTTT CTAAAGACGA AGGTGGACGT CACACTCCAT TCTTCAACAA CTACCGTCCA	720
CAATTCTACT TCCGTACAAC TGACGTAACA GGTTCAATCG AACTTCCAGC AGGTACAGAA	780
ATGGTTATGC CTGGTGATAA CGTGACAATC AACGTTGAGT TGATCCACCC AATCGCCGTA	840
GAACAAGGTA CTACTTTCTC AATCCGTGAA GGTGGACGTA CTGTTGGTTC AGGT	894

## (2) INFORMATION FOR SEQ ID NO: 168:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 897 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Thiobacillus cuprinus*

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

AACATGATCA CCGGTGCGGC CCAGATGGAC GGCGCCATCC TGGTCGTGTC CGCCGCCGAC	60
GGCCCCATGC CCCAAACCCG CGAGCACATC CTGCTGGCGC GTCAGGTGGG CGTGCCTAC	120
ATCATCGTGT TCCTCAACAA GTGCGACATG GTCGACGACG CCGAGCTGCT CGAACTCGTC	180
GAGATGGAAG TCGCGAGCT GCTGTCCAAG TACGACTTCC CCGGTGACGA CACCCCCATC	240
ATCAAGGGCT CGGCCAAGCT GGCCCTCGAA GGCGACAAGG GCGAACTGGG CGAAGGCGCC	300
ATTCTCAAGC TGGCCGAGGC CCTGGACACC TACATCCCCA CGCCCGAGCG GGCCGTCGAC	360
GGCGCGTTCC TCATGCCGT GGAAGACGTG TTCTCCATCT CCGGGCGCGG CACGGTGGTC	420
ACCGGGCGTG TGGAGCGCGG CATCATCAAG GTCGGCGAGG AAATCGAGAT TGTCGGCCTC	480
AAGCCCACCC TCAAGACCAC CTGCACCGGC GTGGAAATGT TCAGGAAGCT GCTCGACCAAG	540
GGCCAGGCCG GCGACAACGT CGGCATTTG CTGCGCGCA CCAAGCGCGA GGAAGTCGAG	600
CGCGGCCAGG TGCTGTGCAA ACCCGGCTCG ATCAAGCCCC ACACCCACTT CACCGCCGAG	660

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GTGTACGTGC TGAGCAAGGA CGAGGGCGGC CGCCACACCC CCTTCTTCAA CAACTACCGC	720
CCGCAGTTCT ACTTCCGCAC CACCGACGTC ACCGGCGCCA TCGAACTGCC CAAGGACAAG	780
GAAATGGTCA TGCCCCGGCGA TAATGTGAGC ATCACCGTCA AGCTCATCGC CCCCCATCGCC	840
ATGGAAGAAG GCCTGCGCTT CGCCATCCGC GAAGGCAGGCC GCACCGTCGG CGCCGGC	897

## (2) INFORMATION FOR SEQ ID NO: 169:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 894 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Treponema pallidum*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

AATATGATCA CGGGTGCTGC GCAGATGGAC GGTGGTATTC TCGTCGTGTC TGCGCCTGAC	60
GGCGTTATGC CACAGACGAA GGAGCATCTT CTGCTCGCCC GTCAGGTTGG TGTTCCTCC	120
ATCATTGTTT TTTTGAACAA GGTTGATTTG GTTGATGATC CTGAGTTGCT AGAGCTGGTG	180
GAAGAAAGAGG TGCCTGATGC GCTTGCTGGA TATGGGTTTT CGCGTGAGAC GCCTATCGTC	240
AAGGGGTCTG CGTTTAAAGC TCTGCAGGAT GGCGCTTCCC CGGAGGATGC AGCTTGTATT	300
GAGGAACCTGC TTGCGGCCAT GGATTCTAC TTTGAAGACC CAGTGCCTGA CGACGCAAGA	360
CCTTTCTTGC TCTCTATCGA GGATGTGTAC ACTATTTCTG GGCGTGGTAC CGTTGTCACG	420
GGGCGCATCG AATGTGGGT AATTAGTCTG AATGAAGAGG TCGAGATCGT CGGGATTAAG	480
CCCACTAAGA AAACAGTGGT TACTGGCATT GAGATGTTA ATAAGTTGCT TGATCAGGGAA	540
ATTGCAGGTG ATAACGTGGG GCTGCTTTG CGCGGGGTGG ATAAAAAAAGA GGTTGAGCGC	600
GGTCAGGTGC TTTCTAAGCC CGGTTCTATT AAGCCACACA CCAAGTTGA GGCGCAGATC	660
TACGTGCTCT CTAAGGAAGA GGGTGGCCGT CACAGTCCTT TTTTCAAGG TTATCGTCCG	720
CAGTTTATT TTAGAACTAC TGACATTACC GGTACGATTCTCTTCTGA AGGGGTAGAC	780
ATGGTGAAGC CGGGGGATAA CACCAAGATT ATAGGTGAGC TCATCCACCC GATAGCTATG	840
GACAAGGGTC TGAAGCTTGC GATTCTGAA GGGGGGCGCA CTATTGCTTC TGTT	894

## (2) INFORMATION FOR SEQ ID NO: 170:

(i) SEQUENCE CHARACTERISTICS:

- 153 -

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Ureaplasma urealyticum*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

AATATGATTA CAGGGGCAGC ACAAAATGGAT GGAGCAATT TAGTTATTGC TGCATCTGAT	60
GGGGTTATGG CTCAAACTAA AGAACATATT TTATTAGCAC GTCAAGTTGG TGTTCACAAA	120
ATCGTTGTTT TCTTAAACAA ATGTGATTTC ATGACAGATC CAGATATGCA AGATCTTGT	180
GAAATGGAAG TTCGTGAATT ATTATCTAAA TATGGATTTG ATGGCGATAA CACACCAGTT	240
ATTCGTGGTT CAGGTCTTAA GGCTTAGAA GGAGATCCAG TTTGAGAAGC AAAAATTGAT	300
GAATTAATGG ACGCAGTTGA TTCATGAATT CCATTACCAAG AACGTAGTAC TGACAAACCA	360
TTCTTATTAG CAATTGAAGA TGTATTACACA ATTCAGGAC GTGGTACAGT AGTAACGTGGA	420
CGTGTGAAC GTGGTGTATT AAAAGTTAAT GATGAGGTTG AAATTGTTGG TCTAAAAGAC	480
ACTCAAAAAA CTGTTGTTAC AGGAATTGAA ATGTTTAGAA AATCATTAGA TCAAGCTGAA	540
GCTGGTGATA ATGCTGGTAT TTTATTACGT GGTATTAAAA AAGAAGATGT TGAACGTGGT	600
CAAGTACTTG TAAAACCAGG ATCAATTAAA CCTCACCGTA CTTTACTGC TAAAGTTTAT	660
ATTCTTAAAA AAGAAGAAGG TGGACGTCAT ACACCTATTG TTTCAGGATA CCGTCCACAA	720
TTCTATTTA GAACAACAGA TGTAACAGGT GCTATTCAT TACCTGCTGG TGTTGATTG	780
GTTATGCCAG GTGATGACGT TGAAATGACT GTAGAATTAA TTGCTCCAGT TCGGATTGAA	840
GATGGATCTA AATTCTCAAT CCGTGAAGGT GGTAAAACGT TAGGTCTGATGG T	891

(2) INFORMATION FOR SEQ ID NO: 171:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 909 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Wolinella succinogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

- 154 -

AACATGATTA CAGGTGCTGC TCAAATGGAT GGCGCGATT C TTGTTGTTTC TGC GGCGGAT	60
GGCCCCATGC CCCAAACTAG GGAGCACATT CTTCTTCTC GACAAGTAGG CGTTCCCTTAC	120
ATCGTGGTTT TCTTGAACAA AGAAGATATG GTTGATGACG CTGAGCTTCT TGAGCTTGTT	180
GAAATGGAAG TTAGAGAACT TCTTAGAAC TACGACTTCC CTGGAGATGA CACTCCTATC	240
GTTGCAGGTT CCGCTCTTAA AGCTCTGAA GAGGCTAACG ACCAGGAAAA TGTTGGCGAG	300
TGGGGCGAGA AAGTATTGAA GCTTATGGCT GAGGTTGACC GATATATTCC TACGCCTGAG	360
CGAGATGTGG ATAAGCCTTT CCTTATGCCT GTTGAAGACG TATTCTCCAT CGCGGGTCGT	420
GGAACCGTTG TGACAGGAAG AATTGAAAGA GGC GTGGTTA AAGTCGGTGA CGAAGTAGAA	480
ATCGTTGGTA TCCGAAACAC ACAAAAAACA ACCGTAAC TG GCGTTGAGAT GTTCCGAAAA	540
GAGCTCGACA AGGGTGAGGC GGGTGACAAC GTTGGTGTTC TTTTGAGAGG CACCAAGAAA	600
GAAGATGTTG AGAGAGGTAT GGTTCTTGT AAAATAGTT CTATCACTCC TCACACTAAC	660
TTTGAAGGTG AAGTTTACGT TCTTCCAAA GAGGAAGGCG GACGACACAC TCCATTCTTC	720
AATGGATACC GACCTCAGTT CTATGTTAGA ACTACAGACG TTACCGGTT TATCTCTCTT	780
CCTGAGGGCG TAGAGATGGT TATGCCTGGT GACAACGTTA AGATCAATGT TGAGCTTATC	840
GCTCCTGTAG CCCTCGAAGA GGGAACACGA TT CGCGATCC GTGAAGGTGG TCGAACCGTT	900
GGTGC GGGGT	909

## (2) INFORMATION FOR SEQ ID NO: 172:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:6
- (D) OTHER INFORMATION:/note= "n = inosine"

## (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

## (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION:18
- (D) OTHER INFORMATION:/note= "n = inosine"

- 155 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:

TARTCNGTRA ANGCYTCNAC RCACAT

26

(2) INFORMATION FOR SEQ ID NO: 173:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 173:

TCTTTAGCAG AACAGGATGA A

21

(2) INFORMATION FOR SEQ ID NO: 174:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:

GAATAATTCC ATATCCTCCG

20

**CLAIMS****What is claimed is:**

1. A method using probes and/or amplification primers which are specific, ubiquitous and sensitive for determining the presence and/or amount of nucleic acids:
  - 5 - from a bacterial antibiotic resistance gene selected from the group consisting of *bla<sub>tem</sub>*, *bla<sub>shv</sub>*, *bla<sub>rob</sub>*, *bla<sub>oxa</sub>*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aac6'-Ila*, *aacA4*, *aad(6')*, *vanA*, *vanB*, *vanC*, *msrA*, *satA*, *aac(6')-aph(2")*, *vat*, *vga*, *ermA*, *ermB*, *ermC*, *mecA*, *int* and *sul*, and
    - 10 - from specific bacterial and fungal species selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species,
  - 15 in any sample suspected of containing said bacterial and/or fungal nucleic acids,
  - 20 wherein each of said nucleic acid or variant or part thereof comprises a selected target region hybridizable with said probes or primers;  
said method comprising the following steps: contacting said sample with said probes or primers and detecting the presence and/or amount of hybridized probes or amplified products as an indication of the presence and/or amount of said specific bacterial and/or fungal species and bacterial antibiotic resistance genes.
  2. A method according to claim 1, which further makes use of probes and/or primers which are specific, ubiquitous and sensitive for determining the presence and/or amount of nucleic acids from any bacterium or fungus.
  3. The method of claim 1, which is performed directly from a test sample.
  - 25 4. The method of claim 1, which is performed directly from a test sample consisting of a bacterial and/or fungal culture or suspension.
  5. The method of claim 1, wherein said nucleic acids are all detected under uniform hybridization or amplification conditions.
  - 30 6. The method of claim 1, wherein said nucleic acids are amplified by a method selected from the group consisting of:
    - a) polymerase chain reaction (PCR),
    - b) ligase chain reaction (LCR),
    - c) nucleic acid sequence-based amplification (NASBA),

- d) self-sustained sequence replication (3SR),
- e) strand displacement amplification (SDA),
- f) branched DNA signal amplification (bDNA),
- g) transcription-mediated amplification (TMA),
- 5 h) cycling probe technology (CPT),
- i) nested PCR, and
- j) multiplex PCR.

7. The method of claim 6, wherein said nucleic acids are amplified by PCR.
8. The method of claim 7, wherein the PCR protocol achieves within one hour  
10 under uniform amplification conditions the determination of the presence of said nucleic acids by performing for each amplification cycle an annealing step of thirty seconds at 45-55°C and a denaturation step of only one second at 95°C without any time specifically allowed to an elongation step.
9. A method for the detection, identification and/or quantification of a  
15 microorganism selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, directly from  
20 a test sample or from bacterial and/or fungal cultures, which comprises the following steps:
  - a) depositing and fixing on an inert support or leaving in solution the said microorganism DNA of the sample or of a substantially homogeneous population of said microorganism isolated from this sample, or  
inoculating said sample or said substantially homogeneous population of  
25 microorganism isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or said isolated microorganism to release the said microorganism DNA,  
said microorganism DNA being made in a substantially single-stranded form;
  - b) contacting said single-stranded DNA with a probe, said probe comprising at  
30 least one single-stranded nucleic acid which nucleotide sequence is selected from the group consisting of SEQ ID NOs: 26, 27, 28, 29, 30, 120, 131 to 134, 31, 140 to 143, 32 to 36, 120 to 124, a sequence complementary thereof, a part thereof having at least 12 nucleotides in length, and a variant thereof, which specifically and ubiquitously anneals with strains or representatives of *Enterococcus faecium*, *Listeria*

5 *monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, respectively, under conditions such that the nucleic acid of said probe can selectively hybridize with  
5 said microorganism DNA, whereby a hybridization complex is formed; and

c) detecting the presence of said hybridization complex on said inert support or in said solution as an indication of the presence and/or amount of said microorganism, in said test sample.

10 10. A method for detecting the presence and/or amount of a microorganism selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, in a test sample which comprises the following steps:

15 a) treating said sample with an aqueous solution containing at least one pair of oligonucleotide primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said microorganism DNA that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NOs: 26, 27, 28, 29, 30, 120, 131 to 134, 31, 140 to 143, 32 to 36, 120 to 20 124, respectively with regard to said microorganism, a sequence complementary thereof, and a variant thereof;

25 b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and

30 c) detecting the presence and/or amount of said amplified target sequence as an indication of the presence and/or amount of said microorganisms, in said test sample.

11. The method of claim 10, wherein said pair of primers is defined in SEQ ID NOs: 1 and 2, 3 and 4, 5 and 6, 7 and 8, 9 and 10, 11 and 12, 13 and 14, 15 and 16, 17 to 20, 21 and 22, respectively, for each of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species and *Streptococcus* species.

12. A method for detecting the presence and/or amount of any bacterium directly from a test sample or a bacterial culture, which comprises the following steps:

- a) depositing and fixing on an inert support or leaving in solution the bacterial DNA of the sample or of a substantially homogeneous population of bacteria isolated 5 from this sample, or
  - inoculating said sample or said substantially homogeneous population of bacteria isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or isolated bacteria to release the bacterial DNA,
    - said bacterial DNA being made in a substantially single-stranded form;
- 10 b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleic acid which nucleotide sequence is selected from the group consisting of SEQ ID NOs: 118, 119, 125 to 171, a sequence complementary thereof, a part thereof having at least 12 nucleotides in length, and a variant thereof, which specifically and ubiquitously anneals with strains or representatives of any 15 bacterial species, under conditions such that the nucleic acid of said probe can selectively hybridize with said bacterial DNA, whereby a hybridization complex is formed; and
  - c) detecting the presence of said hybridization complex on said inert support or in said solution as an indication of the presence and/or amount of any bacterium in 20 said test sample.

13. A method for detecting the presence and/or amount of any bacterium in a test sample which comprises the following steps:

- a) treating said sample with an aqueous solution containing at least one pair of oligonucleotide primers having at least 12 nucleotides in length, one of said primers 25 being capable of hybridizing selectively with one of the two complementary strands of any bacterial DNA that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NO: 30 118, 119, 125 to 171, a sequence complementary thereof, and a variant thereof;
- b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and
  - c) detecting the presence and/or amount of said amplified target sequence as 35 an indication of the presence and/or amount of any bacterium in said test sample.

14. The method of claim 13, wherein said pair of primers is defined in SEQ ID NOs: 23 and 24.

15. A method for obtaining *tuf* sequences from any bacterium directly from a test sample or a bacterial culture, which comprises the following steps:

5 a) treating said sample with an aqueous solution containing a pair of primers having a sequence selected within the nucleotide sequences defined in SEQ ID NOs: 107 and 108, a part thereof having at least 12 nucleotides in length, a sequence complementary thereof, and a variant thereof, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said bacterial *tuf* gene that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template;

10 b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, 15 to a detectable level; and

c) detecting the presence and/or amount of said amplified target sequence; and

d) determining the nucleotide sequence of the said amplified target sequence by using any DNA sequencing method.

16. A method for detecting the presence and/or amount of any fungus directly from 20 a test sample or a fungal culture, which comprises the following steps:

a) depositing and fixing on an inert support or leaving in solution the fungal DNA of the sample or of a substantially homogeneous population of fungi isolated from this sample, or

25 inoculating said sample or said substantially homogeneous population of fungi isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or isolated fungi to release the fungal DNA,

said fungal DNA being made in a substantially single-stranded form;

30 b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleotide sequence selected from the group consisting of SEQ ID NOs: 120 to 124, a sequence complementary thereof, a part thereof having at least 12 nucleotides in length, and a variant thereof, which specifically and ubiquitously anneals with strains or representatives of any fungus, under conditions such that the nucleic acid of said probe can selectively hybridize with said fungal DNA, whereby a hybridization complex is formed; and

35 c) detecting the presence of said hybridization complex on said inert support or

in said solution as an indication of the presence and/or amount of any fungus in said test sample.

17. A method for detecting the presence and/or amount of any fungus in a test sample which comprises the following steps:

5        a) treating said sample with an aqueous solution containing at least one pair of oligonucleotide primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of any fungal DNA that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product  
10      which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NOs: 120 to 124, a sequence complementary thereof, and a variant thereof;

15      b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and

15      c) detecting the presence and/or amount of said amplified target sequence as an indication of the presence and/or amount of any fungus in said test sample.

18. A method for obtaining *tuf* sequences from any fungus directly from a test sample or a fungal culture, which comprises the following steps:

20      a) treating said sample with an aqueous solution containing a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 109 and 172, a part thereof having at least 12 nucleotides in length, a sequence complementary thereof, and a variant thereof, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said fungal *tuf* gene that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template;  
25      b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and

30      c) detecting the presence and/or amount of said amplified target sequence; and

30      d) determining the nucleotide sequence of the said amplified target sequence by using any DNA sequencing method.

19. A method as defined in claim 1, which comprises the evaluation of the presence  
35      of a bacterial resistance mediated by a bacterial antibiotic resistance gene selected

from the group consisting of *bla<sub>oxo</sub>*, *blaZ*, *aac6'-Ila*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*, directly from a test sample or a bacterial culture, which comprises the following steps:

5 a) depositing and fixing on an inert support or leaving in solution the bacterial DNA of the sample or of a substantially homogeneous population of bacteria isolated from this sample, or

inoculating said sample or said substantially homogeneous population of bacteria isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or isolated bacteria to release the bacterial DNA,

said bacterial DNA being made in a substantially single-stranded form;

10 b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleotide sequence having at least 12 nucleotide in length is selected from the group consisting of SEQ ID NOs: 110, 111, 112, 113, 114 115, 116, 117, a sequence complementary thereof, and a variant thereof, which specifically hybridizes with said bacterial antibiotic resistance gene, respectively; and

15 c) detecting the presence of a hybridization complex as an indication of a bacterial resistance mediated by said one of said bacterial antibiotic resistance genes.

20. A method as defined in claim 1, which comprises the evaluation of the presence of a bacterial resistance mediated by a bacterial antibiotic resistance gene selected from the group consisting of *bla<sub>oxo</sub>*, *blaZ*, *aac6'-Ila*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*, directly from a test sample or a bacterial culture, which comprises the following steps:

25 a) treating said sample with an aqueous solution containing at least one pair of primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said bacterial antibiotic resistance gene that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NOs: 110, 111, 112, 113, 114, 115, 116, 117, respectively with regard to said bacterial antibiotic resistance gene, a sequence complementary thereof, and a variant thereof;

30 b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and

35 c) detecting the presence and/or amount of said amplified target sequence as an indication of a bacterial resistance mediated by one of said bacterial antibiotic resistance genes.

21. A method as defined in claim 1, which comprises the evaluation of the presence of a bacterial resistance gene selected from the group consisting of *bla<sub>tem</sub>*, *bla<sub>shv</sub>*, *bla<sub>rob</sub>*, *bla<sub>oxb</sub>*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aac6'-Ila*, *aacA4*, *aad(6')*, *vanA*, *vanB*, *vanC*, *msrA*, *satA*, *aac(6')-aph(2")*, *vat*, *vga*, *ermA*, *ermB*, *ermC*, *mecA*, *int* and *sul*, directly from a test sample or a bacterial culture, which comprises the following steps:

5      a) treating said sample with an aqueous solution containing at least one pair of primers having a sequence selected in the group consisting of SEQ ID NOs: 37 to 40, 41 to 44, 45 to 48, 49 and 50, 51 and 52, 53 and 54, 55 and 56, 57 and 58, 59 to 60, 61 to 64, 65 and 66, 173 and 174, 67 to 70, 71 to 74, 75 and 76, 77 to 80, 81 and 82, 10 83 to 86, 87 and 88, 89 and 90, 91 and 92, 93 and 94, 95 and 96, 97 and 98, 99 to 102, 103 to 106, a part thereof having at least 12 nucleotides in length, a sequence complementary thereof, a variant thereof, and mixtures thereof, one of said primers of said pair being capable of hybridizing selectively with one of the two complementary strands of its respective bacterial antibiotic resistance gene that contains a target 15 sequence, and the other of said primers of said pairs being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template;

15      b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, 20 to a detectable level; and

20      c) detecting the presence and/or amount of said amplified target sequence as an indication of a bacterial resistance mediated by one of said bacterial antibiotic resistance genes.

22. A nucleic acid having the nucleotide sequence of any one of SEQ ID NOs: 26 to 36, 110 to 171, a part thereof, a sequence complementary thereof, and variant thereof which, when in single-stranded form, ubiquitously and specifically hybridizes with a target bacterial or fungal DNA as a probe or as a primer.

25. An oligonucleotide having the nucleotide sequence of any one of SEQ ID NOs: 1 to 25, 37 to 109, 172 to 174, a part thereof, a sequence complementary thereof, and 30 variant thereof, which ubiquitously and specifically hybridizes with a target bacterial or fungal DNA as a probe or as a primer.

30. A recombinant plasmid comprising a nucleic acid as defined in claim 22.

35. A recombinant host which has been transformed by a recombinant plasmid according to claim 24.

35. 26. A recombinant host according to claim 25 wherein said host is *Escherichia coli*.

35. 27. A diagnostic kit for the detection and/or quantification of the nucleic acids of any

combination of the microbial species and/or genera selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, comprising any suitable combination of probes of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 26 to 36, 120 to 124, 131 to 134, 140 to 143, sequences complementary thereof, and variants thereof.

28. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the microbial species and/or genera selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, comprising any suitable combination of primers of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 26 to 36, 120 to 124, 131 to 134, 140 to 143, sequences complementary thereof, and variants thereof.

29. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the microbial species and/or genera selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species and *Streptococcus* species, comprising any suitable combination of primers selected from the group consisting of SEQ ID NOs: 1 to 22, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof.

30. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the bacterial resistance genes selected from the group consisting of *bla<sub>oxb</sub>*, *blaZ*, *aac6'-Ila*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*, comprising any suitable combination of probes of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof.

31. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the bacterial resistance genes selected from the group consisting of *bla<sub>oxb</sub>*, *blaZ*, *aac6'-Ila*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*, comprising any suitable combination of primers of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof.

32. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the bacterial resistance genes selected from the group consisting of *bla<sub>tem</sub>*, *bla<sub>shv</sub>*, *bla<sub>rbp</sub>*, *bla<sub>oxb</sub>*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aac6'-Ila*, *aacA4*, *aad(6')*, *vanA*, *vanB*, *vanC*, *msrA*, *satA*, *aac(6')-aph(2")*, *vat*, *vga*, *ermA*, *ermB*, *ermC*, *mecA*, 5 *int* and *sul*, comprising any suitable combination of primers selected from the group consisting of SEQ ID NOs: 37 to 106, 173 and 174, a part thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof.

10 A diagnostic kit for the detection and/or quantification of the nucleic acids of any bacterium and/or fungus, comprising any combination of probes of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof.

15 34. A diagnostic kit for the detection and/or quantification of the nucleic acids of any bacterium and/or fungus, comprising any suitable combination of primers of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof.

20 35. A diagnostic kit for the detection and/or quantification of the nucleic acids of any bacterium, comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof.

25 36. A diagnostic kit, as defined in claim 27, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

30 37. A diagnostic kit, as defined in claim 28, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

35 38. A diagnostic kit, as defined in claim 29, further comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium.

39. A diagnostic kit, as defined in claim 27, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from

the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterial antibiotic resistance gene selected from the group consisting of *bla<sub>oxb</sub>*, *blaZ*, *aac6'-Ila*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*.

5 40. A diagnostic kit, as defined in claim 28, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterial antibiotic resistance gene selected from the group consisting of *bla<sub>oxb</sub>*, *blaZ*, *aac6'-Ila*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*.

10 41. A diagnostic kit, as defined in claim 29, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 37 to 106, 173 and 174, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterial antibiotic resistance gene selected from the group consisting of *bla<sub>tem</sub>*, *bla<sub>rob</sub>*, *bla<sub>shv</sub>*, *bla<sub>oxb</sub>*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aacA4*, *aac6'-Ila*, *aad(6')*, *ermA*, *ermB*, *ermC*, *mecA*, *vanA*, *vanB*, *vanC*, *satA*, *aac(6')-aph(2")*, *vat*, *vga*, *msrA*, *sul* and *int*.

15 42. A diagnostic kit, as defined in claim 30, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

20 43. A diagnostic kit, as defined in claim 31, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

25 44. A diagnostic kit, as defined in claim 32, further comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium.

30 45. A diagnostic kit, as defined in claim 39, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic

acids of any bacterium and/or fungus.

46. A diagnostic kit, as defined in claim 40, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences 5 complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

47. A diagnostic kit, as defined in claim 41, further comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences 10 complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium.



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> :  C12Q 1/68		A3	(11) International Publication Number: <b>WO 98/20157</b>  (43) International Publication Date: 14 May 1998 (14.05.98)
<p>(21) International Application Number: PCT/CA97/00829</p> <p>(22) International Filing Date: 4 November 1997 (04.11.97)</p> <p>(30) Priority Data: 08/743,637 4 November 1996 (04.11.96) US</p> <p>(71) Applicant (for all designated States except US): INFECTIO DIAGNOSTIC (I.D.I.) INC. [CA/CA]; 4ème étage, 2050, boulevard René Lévesque Ouest, Sainte-Foy, Québec G1V 2K8 (CA).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): BERGERON, Michel, G. [CA/CA]; 2069, rue Brûlard, Sillery, Québec G1T 1G2 (CA). PICARD, François, J. [CA/CA]; 1245, rue de la Sapinière, Cap-Rouge, Québec G1Y 1A1 (CA). OUELLETTE, Marc [CA/CA]; 1035 de Ploerme, Sillery, Québec G1S 3S1 (CA). ROY, Paul, H. [US/US]; 28, rue Charles Garnier, Loretteville, Québec G2A 2X8 (CA).</p> <p>(74) Agents: DUBUC, Jean, H. et al.; Goudreau Gage Dubuc &amp; Martineau Walker, The Stock Exchange Tower, Suite 3400, 800 Place Victoria, P.O. Box 242, Montreal, Québec H4Z 1E9 (CA).</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b> With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</p> <p>(88) Date of publication of the international search report: 13 August 1998 (13.08.98)</p>	
<p>(54) Title: SPECIES-SPECIFIC, GENUS-SPECIFIC AND UNIVERSAL DNA PROBES AND AMPLIFICATION PRIMERS TO RAPIDLY DETECT AND IDENTIFY COMMON BACTERIAL AND FUNGAL PATHOGENS AND ASSOCIATED ANTI-BIOTIC RESISTANCE GENES FROM CLINICAL SPECIMENS FOR DIAGNOSIS IN MICROBIOLOGY LABORATORIES</p> <p>(57) Abstract</p> <p>DNA-based methods employing amplification primers or probes for detecting, identifying, and quantifying in a test sample DNA from (i) any bacterium, (ii) the species <i>Streptococcus agalactiae</i>, <i>Staphylococcus saprophyticus</i>, <i>Enterococcus faecium</i>, <i>Neisseria meningitidis</i>, <i>Listeria monocytogenes</i> and <i>Candida albicans</i>, and (iii) any species of the genera <i>Streptococcus</i>, <i>Staphylococcus</i>, <i>Enterococcus</i>, <i>Neisseria</i> and <i>Candida</i> are disclosed. DNA-based methods employing amplification primers or probes for detecting, identifying, and quantifying in a test sample antibiotic resistance genes selected from the group consisting of <i>bla<sub>tem</sub></i>, <i>bla<sub>rob</sub></i>, <i>bla<sub>shv</sub></i>, <i>bla<sub>oxa</sub></i>, <i>bla<sub>Z</sub></i>, <i>aadB</i>, <i>aacC1</i>, <i>aacC2</i>, <i>aacC3</i>, <i>aacA4</i>, <i>uacB'-Ila</i>, <i>ermA</i>, <i>ermB</i>, <i>ermC</i>, <i>mecA</i>, <i>vanA</i>, <i>vanB</i>, <i>vanC</i>, <i>satA</i>, <i>aac(6'-aph(2'')</i>, <i>aad(6')</i>, <i>vat</i>, <i>vga</i>, <i>msrA</i>, <i>sul</i> and <i>int</i> are also disclosed. The above microbial species, genera and resistance genes are all clinically relevant and commonly encountered in a variety of clinical specimens. These DNA-based assays are rapid, accurate and can be used in clinical microbiology laboratories for routine diagnosis. These novel diagnostic tools should be useful to improve the speed and accuracy of diagnosis of microbial infections, thereby allowing more effective treatments. Diagnostic kits for (i) the universal detection and quantification of bacteria, and/or (ii) the detection, identification and quantification of the above-mentioned bacterial and fungal species and/or genera, and/or (iii) the detection, identification and quantification of the above-mentioned antibiotic resistance genes are also claimed.</p>			

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# INTERNATIONAL SEARCH REPORT

Int. Application No  
PCT/CA 97/00829

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 6 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category <sup>a</sup>	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 08582 A (BERGERON MICHEL G ;OUELLETTE MARC (CA); ROY PAUL H (CA)) 21 March 1996 see whole document, esp claims 1-3 ---	1-14, 19-38, 40-47
X	FR 2 699 539 A (PASTEUR INSTITUT) 24 June 1994 see whole document, esp. abstract and claims ---	1-8,19, 32 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

<sup>b</sup> Special categories of cited documents :

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- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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Date of the actual completion of the international search

8 June 1998

Date of mailing of the international search report

01.07.98

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## INTERNATIONAL SEARCH REPORT

Intern. Appl. No

PCT/CA 97/00829

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	DUTKA-MALEN S. ET AL.,: "Sequence of the vanC gene of Enterococcus gallinarum BM4174 encoding a D-alanine:D-alanine ligase related protein necessary for vancomycin resistance" GENE, vol. 112, - 1992 pages 53-58, XP002066857 see the whole document & DATABASE EMPRO EMBL AC:M75132 ---	1,19,20, 22,30, 31,39,40
		-/-

**INTERNATIONAL SEARCH REPORT**

Inten. Jnal Application No

PCT/CA 97/00829

**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	US 5 523 205 A (COSSART PASCALE ET AL) 4 June 1996 see the whole document ---	1-9
A,P	EP 0 761 815 A (SANDOZ AG ;SANDOZ LTD (CH); SANDOZ AG (DE)) 12 March 1997 see the whole document & DATABASE GENESEQ DERWENT AC:T87876 ---	1,21
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		-/-

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 97/00829

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/CA 97/00829

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 97/00829

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMPRO EMBL 27 October 1996 YOSHIKAWA H.: XP002067254 AC:D64127 ---	22
X	DATABASE EMPRO EMBL thesis, 8 June 1994 KAMLA V.: XP002067255 AC:Z34275 ---	22
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P,X	EP 0 786 519 A (HUMAN GENOME SCIENCES INC) 30 July 1997 seq id 4 -----	22

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA 97/00829

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-13,19,21-29,32-34,36,41-43,45,46 (partly)

Nucleic acids (SEQ. ID.:1,2,13,14,67-70,51,52, 71-76, 81-86,131-134, 173,174) specific for Enterococcus spp., methods using them, and plasmids, hosts and kits containing them

2. Claims: 1-9,11-13,22-26,29,33,34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ ID.: 3,4, 136-139) specific for Listeria monocytogenes, methods using them, and plasmids, hosts and kits containing them

3. Claims: 1-9,11-13,22-26,29,33,34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ. ID.: 5,6,15,16,162) specific for Neisseria spp., methods using them, and plasmids, hosts and kits containing them

4. Claims: 1-9,11-13,21-26,32-34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ ID.: 7,8,17-20,77-80,89-98, 140-143) specific for Staphylococcus spp., methods using them, and plasmids, hosts and kits containing them

5. Claims: 1-9,11-13,22-26,29,33,34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ. ID.: 9,10,21,22,144-146,167) specific for Streptococcus spp., methods using them, and plasmids, hosts and kits containing them

6. Claims: 1-12,22-29,33,34,36,37,42,43,45,46 (partly), 16, 17 (complete)

Nucleic acids (SEQ ID.: 11,12,120-124) specific for Candida albicans, methods using them, and plasmids, hosts and kits containing them

7. Claims: 14,19,20,30,31,35,38,39,40,44,47 (complete), 23, 32 (partly)

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Nucleic acids (SEQ ID.: 23-24, 99-106, 110-117, 118,119, 125-130, 135, 147-161, 163-166, 168-171) specific for universal detection of bacteria and fungus species, methods using them, and plasmids, hosts and kits containing them

**8. Claims: 15,18 (complete)**

Methods for obtaining tuf sequences by using SEQ ID.: 107,108,109 and 172

# INTERNATIONAL SEARCH REPORT

## Information on patent family members

International Application No

PCT/CA 97/00829

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 9608582	A 21-03-1996	AU 3468195	A 29-03-1996	CA 2199144	A 21-03-1996
		EP 0804616	A 05-11-1997	NO 971111	A 09-05-1997
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